

EXHIBIT 77a

Document title: (2) Adrian H on X: "@DanClintonRN @pash22 @ProfRobHoward @LogarithmicDis @LonSchneiderMD @MadhavThambiset @RenegadeSynapse @nvillain_alz @CorriveauNick @DavidJonesBrain @MemoryDoc @ajlees @PhilAlz @DrTFfromKC @smead2 @AlbertoEspay @Kariem_Ezzat @seb_walsh @EWidera @KasperKepp @Jennife10651535 @eturnermd1 @VincentPlanche @ayton_scott @macesari @schrag_matthew @HHS_ORI @FDACDERDirector @CassavaSciences @CUNY @KatherineMLewin @ClicksAndHisses @NIH @adamfeuerstein It's a totally different issue, but I can assure you that many of those outraged with \$SAVA were also outraged with Aduhelm and FDA shenanigans and skeptical of amyloid Abs. But there's equivalence between that and allegedly completely fake science and an allegedly imaginary drug" / X

Capture URL: https://twitter.com/Adrian_H/status/1712881971347517840

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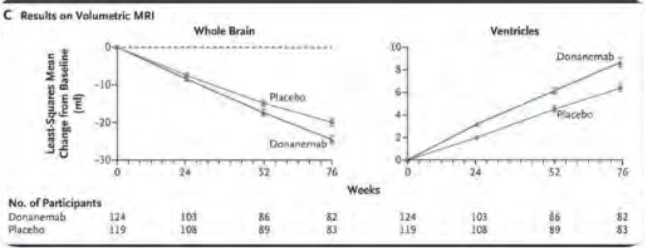
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Madhav Thambisetty @MadhavThambiset · Nov 13, 2022
By this rationale doesn't your own #donanemab cause "neurodegeneration" in #Alzheimers @LillyPad? @ProfRobHoward @pash22 @reshmagar @AlbertoEspay @ayton_scott @gregggonсалves



Madhav Thambisetty @MadhavThambiset · Nov 13, 2022
@LillyPad analysis of #Solanezumab MRI data "Rates of whole brain & ventricular volume changes are sensitive markers of neurodegeneration" tinyurl.com/ebajzwsu
If true, 3 of 4 amyloid abs called "breakthrough Rx" by @US_FDA cause "neurodegeneration" @ProfRobHoward @pash22

1 34 66

Robert Howard @ProfRobHoward · Nov 13, 2022
Goes right back to Nick Fox's 2005 observation that AN1792 caused more volume loss than placebo. Never adequately explained, although I remember fevered discussions about amyloid plaque total volume!



From pubmed.ncbi.nlm.nih.gov

2 3 20

Madhav Thambisetty @MadhavThambiset · Nov 13, 2022
So much of the narrative around these Rx has been on if tiny differences on outcomes are meaningful or not. Almost nothing has been said on how these Rx seem to cause brain atrophy/neurodegeneration. Do consent forms in these trials inform patients about this risk? @nvillain_alz

4 4 16

Nicolas Villain @nvillain_alz · Nov 13, 2022
Clearance of amyloid might lead to decreased microglial activation and/or the reduction of dilated perivascular spaces. 2 factors that, when reduced, will lead to smaller brain volumes measured with T1-w MRI.

4 1 4

Madhav Thambisetty @MadhavThambiset · Nov 13, 2022
Looking at biomarker data from Donanemab tinyurl.com/bdewaf7b decrease in whole brain volume is significantly correlated with NfL levels further suggesting that this is likely due to neurodegeneration.

Jan @810964733763B

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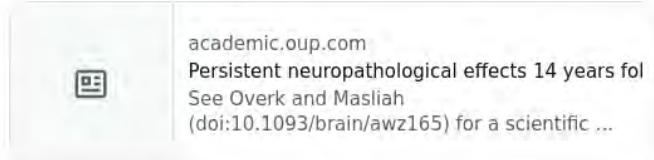
maadnav i nampisetty @maadnav i nampiset · NOV 13, 2022
Looking at biomarker data from Donanemab tinyurl.com/bdewaff7b
decrease in whole brain volume is significantly correlated with NFL levels further suggesting that this is likely due to neurodegeneration.



 **Nicolas Villain** @nvillain_alz · Nov 13, 2022

I know. Still, I maintain my opinion: when inducing changes in the brain clearance system by a drug, as amyloid mAbs do, no one can predict how it will interfere with soluble peripheral biomarkers. I think long-term autopsy in AN1792 are stronger evidence than this correlation.


Madhav Thambisetty @MadhavThambiset · Nov 13, 2022
My reading of the AN1792 postmortem results is that it clearly accelerated disease progression.
"Despite modification of AD pathology, most patients had progressed to severe dementia, notably including the five with very extensive plaque removal"



Robert Howard @ProfRobHoward · Nov 13, 2022
My memory is that the numbers were pretty small compared with those we see in current antibody trials, so may not have had power to show positive or negative effects on disease course.

Ash Paul @pash22 · Nov 13, 2022
It was obviously underpowered but imp to note each & everyone of the five pts with very extensive plaque removal progressed to severe dementia @MemoryDoc @jasonkarlawish @LonSchneiderMD @bartels2

Nicolas Villain @nvillain_alz · Nov 13, 2022
Yes, that's my point: the prognosis did not seem to better (=benefit of the drug), nor worse (=accelerated neurodegeneration) in these patients. But it was, of course, underpowered, so we should remain cautious.

 **Alberto J Espay** @AlbertoEspay · Nov 13, 2022
Power: How many patients with complete clearance of amyloid are needed to demonstrate an effect? Is there a "number needed to treat"?
Opinion: We can always blame lack of effect on unabated progression of tau. No need to take the ACH prediction [amyloid begets tau] literally!


Nicolas Villain @nvillain_alz · Nov 13, 2022

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@810964733763B

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progression or tau. No need to take the ACH prediction [amyloid begets tau] literally!

3 1 4

Nicolas Villain @nvillain_alz · Nov 13, 2022
Opinion: would you throw the baby out with the bathwater? Are the neuropath data from a biased subset of individuals enough to you to disprove the ACH? (even if I prefer Frisoni's probabilistic model, we should remain rigorous when demonstrating or disproving assumptions)

1 2

barttels @barttels2 · Nov 13, 2022
Speaking of water, that metaphor is trying to carry an awful lot of it there.

1 2

Alberto J Espay @AlbertoEspay · Nov 14, 2022
We live with an unfalsifiable amyloid hypothesis. It has failed the "3 main tests", as reviewed in @KarlHerrup's timely book How Not To Study a Disease. We have developed all sorts of intellectual contortions to keep defending a compelling (if false) idea.

1 1 9

Nicolas Villain @nvillain_alz · Nov 14, 2022
Of course, the ACH is disputed. There are alternative propositions in the field, such as @GiovanniFrisoni's probabilistic model that I find very interesting:

nature.com
The probabilistic model of Alzheimer disease: th
Nature Reviews Neuroscience - The amyloid
hypothesis has been the dominant model for ...

2 1 4

Alberto J Espay @AlbertoEspay · Nov 15, 2022
The "probabilistic" model does not refute the ACH, just blames the failures on a "deterministic" interpretation. We will remain on the amyloid-is-toxic bandwagon for another decade, thanks to the aducanumab nail the FDA extracted from what could have been the final ACH coffin.

3 4

Nicolas Villain @nvillain_alz · Nov 15, 2022
There is much evidence regarding the toxicity of some dimensions of amyloid pathology. I know the alternative theory you defend @AlbertoEspay. Unless you demonstrate that all the evidence in favor of amyloid toxicity is flawed, I don't see how you can gather all these... 1/2

1 2

Nicolas Villain @nvillain_alz · Nov 15, 2022
... pieces of evidence together 2/2

1 2

Nicolas Villain @nvillain_alz · Nov 15, 2022
Therefore, I find this probabilistic approach interesting: the problem is not the ACH per se, but its importance. And, therefore, we can gather all the pieces of evidence in a single model.

1 2

Ash Paul @pash22 · Nov 15, 2022
Here's a related cynical tweet from Madhav
twitter.com/MadhavThambise... @macesari @geoperry @samqandy

...

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Adrian H
@Adrian_H
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Madhav Thambisetty @MadhavThambiset · Nov 15, 2022
ANTI-AMYLOID Rx #Alzheimers
Not lowering right amyloid
Not treating early enough
Not treating long enough
Not using right dose...
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Alberto J Espay @AlbertoEspay · Nov 15, 2022
This is why @nvillain_alz's challenge ("Unless you demonstrate that all evidence in favor of amyloid toxicity is flawed...") can never be resolved. Always a bailout. More poignantly, is there an experiment whose outcome can unarguably falsify the ACH?

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Ash Paul @pash22 · Nov 16, 2022
Despite fact that gantenerumab did not significantly lower amyloid, @DrMariaALZ said the studies "further illustrate the relationship between removal of beta-amyloid & reduction of clinical decline", writes @AGKootenay et al
HT @AE_MD [twitter.com/AE_MD/status/1...](#) @Kariem_Ezzat

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Ash Paul @pash22 · Nov 16, 2022
Also, how relevant is this? [science.org/content/blog-p...](#) via @Dereklowe

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Ash Paul @pash22 · Nov 16, 2022
Amyloid and tau PET-positive cognitively unimpaired individuals are at high risk for future cognitive decline [nature.com/articles/s4159...](#) via @RikOssenkoppele et al

[nature.com](#)
Amyloid and tau PET-positive cognitively unimpaired individuals are at high risk for future cognitive decline
Nature Medicine - Abnormal amyloid and tau PET in cognitively unimpaired individuals is ...

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Alberto J Espay @AlbertoEspay · Nov 16, 2022
This one fits in Karl Herrup's "third fallacy:" it amyloid and tau precede cognitive impairment, they must cause it. It is the hardest to break away from. It will keep us on an anti-amyloid and anti-tau crusade for years.

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barttels @barttels2 · Nov 16, 2022
Another 30, heaven forfend?

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Robert Howard @ProfRobHoward · Nov 16, 2022
Could be another 300. Alzheimer's disease is a truly hard problem.

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Adrian H @Adrian_H
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Robert Howard @ProfRobHoward · Nov 16, 2022
Could be another 300. Alzheimer's disease is a truly hard problem.

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barttels @barttels2 · Nov 16, 2022
I was pointing at this hypothesis rather than the entire field. Been known to say, if Henry Marsh doesn't understand the brain, nobody understands the brain.

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Ash Paul @pash22 · Nov 17, 2022
Alzheimer's disease: surprising new theory about what might cause it [theconversation.com/alzheimers-dis...](https://theconversation.com/alzheimers-dis-...) via @andrea_sturchio & @Kariem_Ezzat & @AndaloussiLab



Alzheimer's disease: surprising new theory about what might cause it

From theconversation.com

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barttels @barttels2 · Nov 17, 2022
Just found that a bit ago, read, and followed.

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Ash Paul @pash22 · Nov 17, 2022
The quest to learn if our brain's mutations affect mental health: For years scientists have tried to find a gene for conditions like schizophrenia, Alzheimer's and autism. But the real source could lie in a much more complex genetic puzzle technologyreview.com/2021/08/25/103... via @rkhamisi



The quest to learn if our brain's mutations affect mental health

From technologyreview.com

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barttels @barttels2 · Nov 17, 2022
Intriguing.

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Ash Paul @pash22 · Nov 17, 2022
Another related v interesting paper from @seb_walsh & @r_merrick et al

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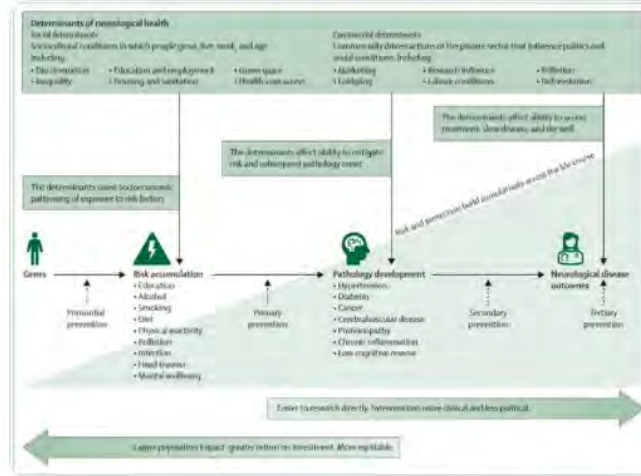


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**Ash Paul** @pash22 · Nov 17, 2022

Another related v interesting paper from @seb_walsh & @r_merrick et al
 "The relevance of social and commercial determinants for neurological health" [the-lancet.com/journals/lanneu...](https://the-lancet.com/journals/lanneu)

**Ash Paul** @pash22 · Nov 17, 2022

Alzheimer's risk gene undermines insulation of brain's "wiring", says @DrLiHueiTsai et al study [picower.mit.edu/news/alzheimer...](https://picower.mit.edu/news/alzheimer)

**Ash Paul** @pash22 · Nov 17, 2022

'We were right all along:' For @EisaiUS, success against Alzheimer's has been a long time coming statnews.com/2022/11/17/we-... via @adamfeuerstein & @Jasonmmast & @damiangarde



From statnews.com

**Ash Paul** @pash22 · Nov 17, 2022

Qs Madhav @MadhavThambiset has asked the @statnews authors, arising out of the 📌 story 📌

**Madhav Thambisetty** @MadhavThambiset · Nov 17, 2022

Replying to @adamfeuerstein

Great reporting as always Adam & @damiangarde Did you also get a chance to ask @EisaiUS CEO about highly statistically significant loss of brain volume across all Rx groups in their phase-2 study? @ProfRobHoward @pash22 🙏

Supplemental Figure S4B. Change from Baseline for Whole Brain Volume (S4B) for All Dosing Groups

**Jan** @810964733763B

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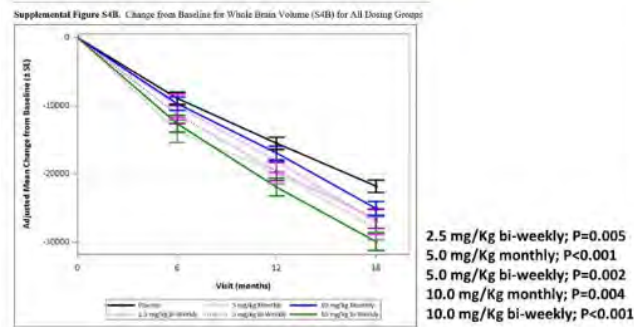
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get a chance to ask @ProfRobHoward @pash22
significant loss of brain volume across all Rx groups in their
phase-2 study? @ProfRobHoward @pash22



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Ash Paul @pash22 · Nov 17, 2022

Is it Alzheimer's? Families want to know, and blood tests may offer answers.

[washingtonpost.com/health/2022/11...](https://www.washingtonpost.com/health/2022/11...) via @lauriemcginley2



From washingtonpost.com

3 2 2



Ali Ezzati @AE_MD · Nov 17, 2022

Wishful thinking: It would be nice if people stop prematurely pushing to use blood based biomarkers for diagnostic purposes in clinical practice. We are at least few years away from having well validated, reliable AD-BBMs.

4 11



barttels @barttels2 · Nov 17, 2022

The "it would be nice" list is *extraordinarily* long.

1 3



Ash Paul @pash22 · Nov 19, 2022

For Alzheimer's Scientists, the Amyloid Debate Has No Easy Answers: For years, potential therapies that attack this brain protein have failed to help patients in clinical trials. Now—surprisingly—a new drug shows promise

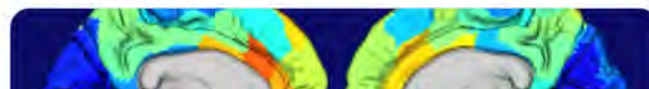
www.wired-com.cdn.ampproject.org/c/s/www.wired.... via @grace_huckins

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Ash Paul @pash22 · Nov 19, 2022

@aylinsdincer Study yields clues to why Alzheimer's disease damages certain parts of the brain source.wustl.edu/2022/11/study-... via @WUSTLdbbs 's #TamaraBhandari



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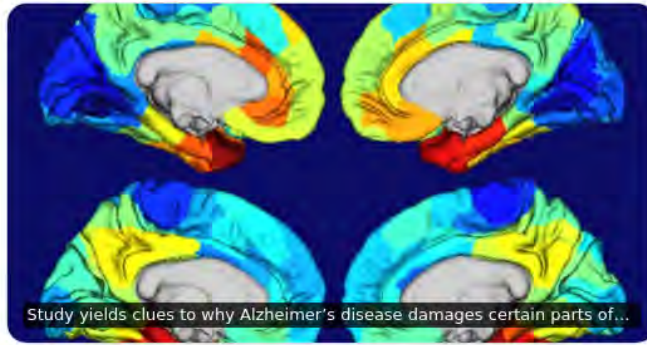
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damages certain parts of the brain source.wustl.edu/2022/11/study-... via [@WUSTLdbbs](#) 's [#TamaraBhandari](#)



From source.wustl.edu

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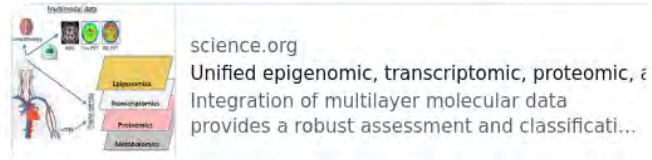
This is interesting.

1 1



Ash Paul @pash22 · Nov 19, 2022

Unified epigenomic, transcriptomic, proteomic, and metabolomic taxonomy of Alzheimer's disease progression and heterogeneity science.org/doi/10.1126/sc... via [@MedInYasser](#) et al



2 2



Ash Paul @pash22 · Nov 19, 2022

Unlocking new clues to how dementia and Alzheimer's work in the brain theconversation.com/unlocking-new-... via [@PaulKeaveny](#) & [@waresgemma](#)



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barttels @barttels2 · Nov 19, 2022

"Itzhaki, a neurobiologist and visiting professorial fellow at the University of Oxford, believes the common cold sore virus (herpes simplex 1 or HSV1) could be playing a vital role in Alzheimer's. But she has faced years of hostility from many within the scientific community ..."

1 2



barttels @barttels2 · Nov 19, 2022

"... who didn't take the theory seriously. Now, though, it seems the tide of opinion is at last turning in Itzhaki's favour."

Not instinctively inclined to believe it, but would be a veritable miracle if it were so identified.

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Robert Howard @ProfRobHoward · Nov 19, 2022

It would be a miracle, indeed.

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Robert Howard @ProfRobHoward · Nov 19, 2022

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· Nov 19, 2022

It would be a miracle, indeed.

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@pash22

· Nov 30, 2022

Alzheimer's Drug May Benefit Some Patients, New Data Shows: Lecanemab, made by @EisaiUS and @biogen, also carried risks of brain swelling and bleeding and should be studied further, a @NEJM report of the findings said [nytimes.com/2022/11/29/hea...](https://www.nytimes.com/2022/11/29/health/alzheimers-drug-lecanemab.html) via @PamBelluck

Published 2022



Alzheimer's Drug May Benefit Some Patients, New Data Shows (Publish...

From nytimes.com

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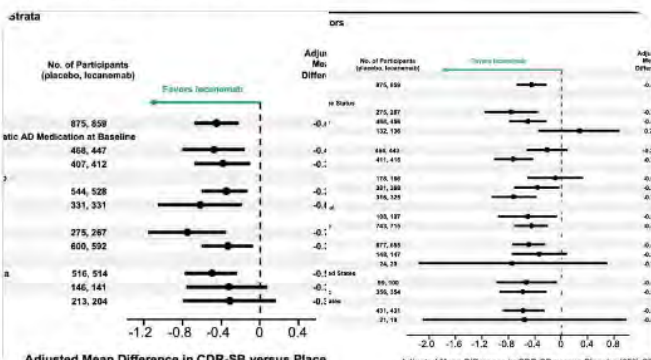
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Prof Scott Ayton

@ayton_scott

· Nov 30, 2022

The exploratory findings were interesting. Little effect in MCI and younger people (this argues against treating earlier). Effect was also less in e4 carriers (esp e4e4) and women. I wonder if less effect is related to ARIA or volume loss?



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Prof Scott Ayton

@ayton_scott

· Nov 30, 2022

Note the risk of ARIA-E in e4/e4: 32.6% vs 10.9% in e4 heterozygotes and 5.4 % in non-carriers. This marked difference could well explain the relatively poor performance of e4/e4 on lecanemab.

	Placebo (N=897) n/N (%)	Lecanemab (N=898) n/N (%)
ARIA-E	15/897 (1.7)	113/898 (12.6)
ARIA-E by ApoE4 genotype		
ApoE4 noncarrier	1/286 (0.3)	15/278 (5.4)
ApoE4 carrier	14/611 (2.3)	98/620 (15.8)
ApoE4 heterozygote	9/478 (1.9)	52/479 (10.9)
ApoE4 homozygote	5/133 (3.8)	46/141 (32.6)

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ApoE4 carrier	14/611 (2.3)	98/620 (15.8)
ApoE4 heterozygote	9/478 (1.9)	52/479 (10.9)
ApoE4 homozygote	5/133 (3.8)	46/141 (32.6)

Ash Paul @pash22 · Dec 1, 2022
Tweeetorial on Lecanemab from Matthew @schrag_matthew
[twitter.com/schrag_matthew...](#) @kathy_y_liu

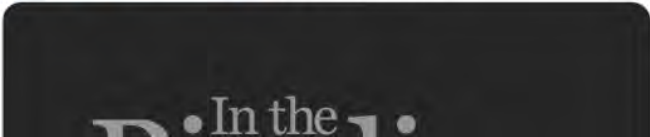
Matthew Schrag @schrag_matthew · Nov 30, 2022
My thoughts on the phase 3 results of Alzheimer's drug lecanemab from Biogen and Eisai, presented at #CTAD #CTAD22 and published this evening in the @NEJM. Major takeaway - this is NOT the breakthrough we have been waiting for. Key points:



Ash Paul @pash22 · Dec 1, 2022
Further Qs on Lecanemab from Kariem @Kariem_Ezzat
[twitter.com/Kariem_Ezzat/s...](#) @dmrind @icer_review

Kariem Ezzat @Kariem_Ezzat · Dec 1, 2022
Besides the clinical questions about #lecanemab, there're also important basic science questions. It's supposed to be an oligomer/protofibril targeting antibody, which isn't assessed at all in the results. Also, it removes the plaques, are they the toxic species? Do plaques..1/2

Ash Paul @pash22 · Dec 1, 2022
"Regarding results for lecanemab, I think that the numbers are the best that I have yet seen for such an antibody, and at the same time I doubt if the drug will actually make a difference in the treatment of Alzheimer's"
[science.org/content/blog-p...](#) via @Dereklowe



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From science.org

2 2 8

Ash Paul @pash22 · Dec 1, 2022

@Biogen stock falls on report that patient died in @EisaiUS 's Alzheimer trial

bostonglobe.com/2022/11/28/bus... via @naomikresge

bostonglobe.com

Biogen stock falls on report that patient died in I Shares for the Cambridge-based company fell as much as 4.9 percent Monday in New York, ...

2 1 5

barttels @barttels2 · Dec 1, 2022

"Rudolph Castellani, a neuropathologist at Northwestern University who investigated the death, blamed it on the 'one-two punch' of lecanemab and the anti-clotting drug, called tPA.

"There's zero doubt in my mind that this is a treatment-caused illness and death."

1 3

Ash Paul @pash22 · Dec 2, 2022

According to Nicolas @nvillain_alz , @DrMariaALZ has said this twitter.com/nvillain_alz/s...

Presumably @alzassociation will then be paying for the drug if her populist argument is accepted by @US_FDA & @CMSSGov ??????????

Nicolas Villain @nvillain_alz · Dec 1, 2022

Replying to @CaroleDufouil @SFackley and 2 others

"The risk/benefit should be assessed by the patients and relatives, not regulators, payors, or physicians" Dr. Maria Carillo —> of course: with a well-published positive phase 3 trial, why do we need regulators?? Let's destroy the agencies!

1 1 4

barttels @barttels2 · Dec 2, 2022

She lost all her credibility on Aduhelm, as far as I'm concerned.

This just underscores it and adds some exclamation points.

1 8

Ash Paul @pash22 · Dec 2, 2022

As a clinical payer, I'm really worried about these types of irresponsible statements from clinical leaders. Yes, we absolutely need to have shared decision making, but NO, we don't absolutely want the abolition of regulators and payers (COI ie I am a clinical payer)

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irresponsible statements from clinical leaders. res, we absolutely need to have shared decision making, but NO, we don't absolutely want the abolition of regulators and payers (COI ie I am a clinical payer)

1 10



Ash Paul @pash22 · Dec 2, 2022
Relevant tweet from Mike @ideapharma on the subject HT @bartels2



Mike Rea, IDEA Pharma @ideapharma · Dec 2, 2022
Great to see this out in the wild - as Ed Cox reminded us at this year's @CNSSummit, @akalali suggested a Nobel Prize should be on the way if this works...
firstwordhealthtech.com/story/5681941
@brent_vaughan @cognitotx Improvement, slowing of atrophy...

1 3

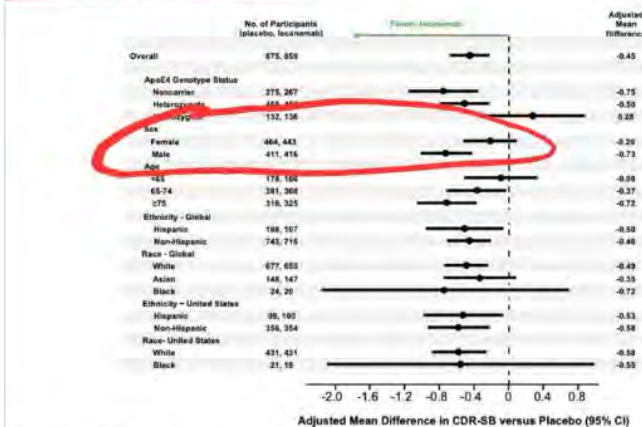


Ash Paul @pash22 · Dec 2, 2022
Interesting tweet from Rachel @bucklr01



Rachel Buckley @bucklr01 · Dec 1, 2022
Everyone's talking about the phase 3 results of #Alzheimers drug Lecanemab presented at #CTAD #CTAD22 and published this evening in the @NEJM. But a really striking subgroup analysis that no one else has pointed out yet (cred. @RoreBole) is that the findings are driven by men!

ty AD Subgroup Analyses: CDR-SB istent Results Across Other Subgroups of Interest



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Ash Paul @pash22 · Dec 2, 2022
An @AnavexLifeSci study spin job sullies an otherwise spectacular Alzheimer's conference statnews.com/2022/12/02/an-... via @adamfeuerstein



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An Anavex study spin job sullies an otherwise spectacular Alzheimer's c...

From statnews.com

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barttels @barttels2 · Dec 2, 2022
Yeeikes!!!

"Slowed the rate of cognitive decline—by changing the study's primary efficacy goals, omitting patients from the analysis, randomly altering data, making basic math errors, whistling past safety concerns, and using nonsensical statistical tests."

1 4

barttels @barttels2 · Dec 2, 2022
Cannot figure out why investors don't like him. 🤔🤔🤔

1 3

Ash Paul @pash22 · Dec 3, 2022
Alzheimer's researchers try out an unfamiliar sensation: optimism
statnews.com/2022/12/02/alz... via [@JonathanWosen](#) & [@damiangarde](#)

statnews.com

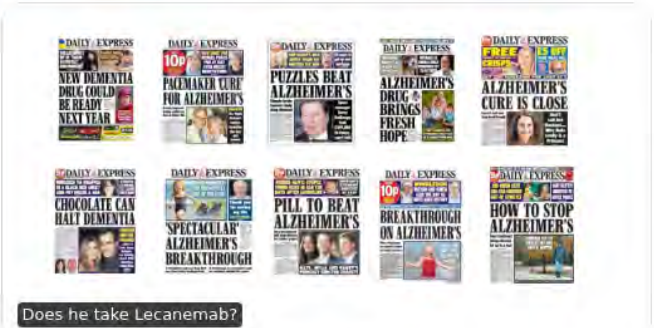
Alzheimer's researchers try out an unfamiliar se

Scientific meetings about Alzheimer's disease

can be funereal affairs. But this year's Clinical...

1 2 2

Ash Paul @pash22 · Dec 3, 2022
Does he take Lecanemab?
makingrightsmakesense.wordpress.com/2022/12/01/doe... via [@neilmcrowther](#)



Does he take Lecanemab?

From makingrightsmakesense.wordpress.com

2 4 5

Ash Paul @pash22 · Dec 3, 2022
[@alzassociation](#), which is also a staunch supporter of aducanumab, called on [@CMSGov](#) to cover the drug if [@US_FDA](#) approves it. It did not address the drug's potential high cost, the adverse effects, or the two reported deaths, writes [@rdotinga](#) in [@Medscape](#)

barttels @barttels2 · Dec 3, 2022
"The Alzheimer's Association raved about lecanemab and declared that the FDA should approve lecanemab on an accelerated basis."

Surprise! 🤔🤔🤔...

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@810964733763B

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"The Alzheimer's Association raved about lecanemab and declared that the FDA should approve lecanemab on an accelerated basis."
Surprise! 🤔🤔🤔...
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Alberto J Espay @AlbertoEspay · Dec 3, 2022
How did the [@alzassociation](#) turn into a political force? Was it always an arm of industry, masked behind patient advocacy?

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Timothy Daly, PhD @PhilAlz · Dec 4, 2022
Here's a good paper on the history of the AA

As a library, the National Library of Medicine (NLM) provides access to scientific literature.

Inclusion in an NLM database does not imply endorsement of, or agreement with, the contents by NLM or the National Institutes of Health.

Trust at stake: Is the "dual mission" of the U.S. Alzheimer's Association ...

From [pubmed.ncbi.nlm.nih.gov](#)

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barttels @barttels · Dec 4, 2022
That piece is dead-on about long term "care" facilities and the unfortunate people who staff them.

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Ash Paul @pash22 · Dec 6, 2022
Lecanemab for Alzheimer's disease: tempering hype and hope
[sciencedirect.com/science/articl...](#) via [@TheLancet](#)

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Ash Paul @pash22 · Dec 6, 2022
Assessing the Preparedness of the U.S. Health Care System: Infrastructure for an Alzheimer's Treatment
[rand.org/pubs/research...](#) via [@jodilliu](#) et al & [@RANDCorporation](#)

rand.org

U.S. Health System Should Prepare for Future AI: The U.S. health care system isn't ready to meet demand for a breakthrough Alzheimer's ...

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Ash Paul @pash22 · Dec 6, 2022
How will [@CMSGov](#) cover Lecanemab funding, if /when it is approved by [@US_FDA](#) ?
Lon [@LonSchneiderMD](#) speculates [👇](#)

Lon S. Schneider, MD @LonSchneiderMD · Dec 4, 2022
Replying to [@ProfRobHoward](#)
The way CMS will both cover & throttle #lecanemab use: Will cover the PET if u qualify for it, based on seeing a specialist, if u can find one, if u can schedule the PET, if u pass, if u find an

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 **Jan** @810964733763B ...

Lon S. Schneider, MD @LonSchneiderMD · Dec 4, 2022

Replying to @ProfRobHoward

The way CMS will both cover & throttle #lecanemab use: Will cover the PET if u qualify for it, based on seeing a specialist, if u can find one, if u can schedule the PET, if u pass, if u find an infusion ctr, if they have drug, if u have \$20K, if u still want it. ... [Show more](#)

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Robert Howard @ProfRobHoward · Dec 6, 2022

Worth reading the RAND report in full. Here's the summary.

- Alzheimer's disease is a progressive neurodegenerative disorder that leads to cognitive decline, dementia, and premature death. No disease-modifying treatment is available but encouraging results from clinical trials offer hope that one or more therapies will become available as early as 2020.
- This prospect raises the question of whether the U.S. health care system is prepared to handle the expected large number of patients. Around 15 million Americans with mild cognitive impairment, which could be an early sign of the disease, will have to be evaluated by specialists, undergo diagnostic testing, and be treated.
- A simulation analysis shows that projected capacity is insufficient to handle the expected case load and predicts patients would have to wait an average of 18.6 months for treatment in 2020. Approximately 2.1 million patients would develop Alzheimer's dementia between 2020 and 2040 while on waiting lists.
- The most pressing constraint is limited capacity of specialists to evaluate and diagnose patients, but access to imaging to confirm Alzheimer's disease and to infusion centers to deliver the treatment would also contribute to waiting times.
- Addressing capacity constraints requires solving a complex puzzle consisting of payment policy, regulatory requirements, workforce considerations, and capacity planning at the national and local levels, combined with awareness campaigns.
- No individual stakeholder will be able to put all the pieces

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Seb Walsh @seb_walsh · Dec 6, 2022

Investing in imaging capacity before we have meaningful treatments is like trying to run before you can crawl...

...with significant opportunity cost...

...and then there's the ethics...

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Robert Howard @ProfRobHoward · Dec 6, 2022

We saw with cancer that this investment can happen once you have treatments that really make a difference to quality of life and survival.

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Seb Walsh @seb_walsh · Dec 6, 2022

The other pertinent comparison is hitting earlier in disease process ('pre-cancerous' change etc.). Need clear evidence of net benefit for intervening for people who may never suffer symptoms.

Is asymptomatic amyloid more PSA for prostate, or more HPV for cervix? Ditto MCI

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Nicolas Villain @nvillain_alz · Dec 6, 2022

That's exactly what we debate in our 2021 TLN paper!!



thelancet.com

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Nicolas Villain @nvillain_alz · Dec 6, 2022
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thelancet.com
Clinical diagnosis of Alzheimer's disease: recom
In 2018, the US National Institute on Aging and the Alzheimer's Association proposed a purel...

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Ash Paul @pash22 · Dec 6, 2022
We recommend "biomarker-positive cognitively unimpaired individuals should be considered only at-risk for progression to Alzheimer's disease" How many will progress to the disease? On top of that, how validated are the biomarkers?

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Ash Paul @pash22 · Dec 6, 2022
As a clinical payer, concerned with unnecessary harm to the pt, I am reminded of the analogy with incidentalomas and also abt the dreaded 'cascade of care'
"The Important but Rarely Studied Cascade of Care"
jamanetwork.com/journals/jaman... via @drjohnm & @dr_dmorgan

jamanetwork.com
The Important but Rarely Studied Cascade of Ca
While technology has greatly improved health care, its advances are not free of downsides. ...

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Ash Paul @pash22 · Dec 6, 2022
Also chk out "Cascades of Care After Incidental Findings in a US National Survey of Physicians"
researchgate.net/publication/33... via @lshaniG & @greyscalespaces et al

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Alberto J Espay @AlbertoEspay · Dec 6, 2022
About the "at risk" situation coming from positive testing: five times

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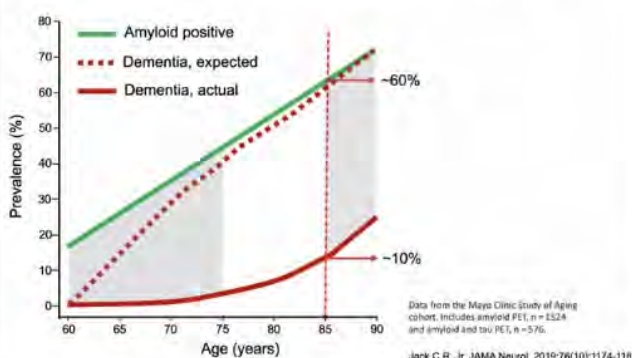
**Alberto J Espay** @AlbertoEspay · Dec 6, 2022

About the "at risk" situation coming from positive testing: five times more of us will be amyloid PET positive but won't develop Alzheimer's disease within our life span.

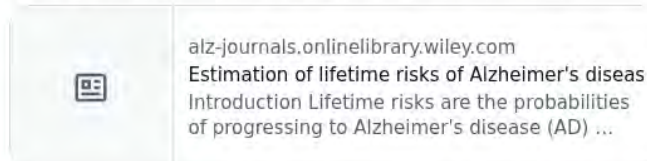
**Alberto J Espay** @AlbertoEspay · Mar 21, 2021

Replying to @AlbertoEspay

(9/10) Brain amyloid accumulates linearly as we age. If it were toxic, the ratio of amyloid-positivity to dementia would approach 1 toward the end of a normal life span. Instead, by age 85, there is a five-fold lower prevalence of dementia than predicted.

**Nicolas Villain** @nvillain_alz · Dec 6, 2022

We need quantified epidemiological from prospective cohorts data to establish that. It's actually been available for a few years (and data keep accumulating) and there is no doubt that amyloid positivity is a risk factor (or marker) of cognitive decline

**Seb Walsh** @seb_walsh · Dec 7, 2022

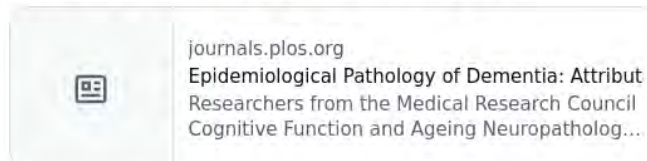
But vital context:

Most cognitively unimpaired people with amyloid positivity will not get dementia in lifetime (your paper).

And most dementia mortality not attributable to amyloid (this paper)

journals.plos.org/plosmedicine/a...

Take home: amyloid assoc but not the be all and end all

**Nicolas Villain** @nvillain_alz · Dec 7, 2022

Absolutely: necessary (without amyloid pathology, no AD), but not sufficient!



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@pash22

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Nicolas Villain @nvillain_alz · Dec 7, 2022
Absolutely: necessary (without amyloid pathology, no AD), but not sufficient!

Ash Paul @pash22 · Dec 7, 2022
How does @NEJM define 'moderately less' exactly? If there is such a term, does NEJM then have terms like 'mildly less' & 'severely less'? This is getting absolutely ludicrous!

Lon S. Schneider, MD @LonSchneiderMD · Dec 7, 2022
Replying to @LonSchneiderMD
Penultimate sentence in actual @NEJM print:
"In persons with early [AD], lecanemab reduced brain amyloid levels and was associated with less MODERATELY LESS decline on clinical measures of cognition and function ..." [Show more](#)

Ash Paul @pash22 · Dec 8, 2022
Losing the thread: experiences of cognitive decline in Alzheimer's disease cambridge.org/core/journals/... via @ucl's Prof [#PaulBebbington](#)

BJPsych cambridge.org
Losing the thread: experiences of cognitive decline in Alzheimer's disease - Volume 222 ...

barttels @barttels2 · Dec 8, 2022
This is a great piece! I thank him for writing it!

Will be interested if he writes more.

Ash Paul @pash22 · Dec 8, 2022
Yet more hypothetical Qs from Madhav [@MadhavThambiset](#)

Madhav Thambisetty @MadhavThambiset · Dec 8, 2022
If @EisaiUS recommends restricting #lecanemab to E4 non carriers and E4 heterozygous patients to reduce risk of brain bleeding will @US_FDA require APOE genotyping in the prescribing label? @EricTopol @Dereklowe @ProfRobHoward @adamfeuerstein @pash22 @reshmagar @gregggonssalves ... [Show more](#)

Madhav Thambisetty @MadhavThambiset · Dec 8, 2022
Not quite "hypothetical" @statnews reports that Eisai CEO recommends not prescribing #lecanemab to APOE4 homozygous patients tinyurl.com/yfsxssrj to minimize risk of brain bleeding. To me it follows that he recommends APOE genotyping for patients to assess risk of brain bleeds

statnews.com
'This is not a cure': Consensus begins to emerge
Eisai CEO Ivan Cheung and Jason Karlawish of the Penn Memory Center discussed balancing...

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statnews.com
'This is not a cure': Consensus begins to emerge
Eisai CEO Ivan Cheung and Jason Karlawish of the Penn Memory Center discussed balancing...

2 4 10

barttels @barttels2 · Dec 8, 2022
Has anyone claimed it is a cure?
2 1

Nicolas Villain @nvillain_alz · Dec 8, 2022
There's a question mark, and I did not read it, but the overview looks laudatory...
2 2

barttels @barttels2 · Dec 8, 2022
This Anderson Smart character has cranked out a bunch of pamphlets exorbitantly priced per page.
Only two have any reviews, and those on Amazon are one star.
1 1

barttels @barttels2 · Dec 8, 2022
He's no Dale Bredezen (praise jeebus).
1 1

Ash Paul @pash22 · Dec 10, 2022
Informative tweet thread on Lecanemab, initiated by Madhav @MadhavThambiset

Madhav Thambisetty @MadhavThambiset · Dec 10, 2022
How not to present a survival analysis in the world's preeminent medical journal @NEJM when reporting on a new treatment for #Alzheimers @ProfRobHoward @pash22 @eturnermd1 @Dereklowe @EricTopol @gregggonssalves @SFAckley @nvillain_alz @MariaGlymour @ideapharma @JAMANeuro

2 3 12

Ash Paul @pash22 · Dec 11, 2022
Interesting observation on the Lecanemab trial made by Seb @seb_walsh
twitter.com/seb_walsh/stat... Chk out that tweet thread as well

Seb Walsh @seb_walsh · Dec 11, 2022
Replying to @MadhavThambiset @pash22 and 13 others
In other news, they report quality of life outcomes only in press releases and CTAD slides, and not in the paper or appendix.
They are classed as "exploratory analyses" rather than "key ...
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In other news, they report quality of life outcomes only in press releases and CTAD slides, and not in the paper or appendix.

They are classed as "exploratory analyses" rather than "key ...
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6

Ash Paul @pash22 · Dec 12, 2022
Tweeetorial on p-tau biomarkers by @JosephTherr

Joseph Therriault @JosephTherr · Dec 12, 2022

What do fluid p-tau biomarkers reflect?
@vermeiren_marie and I provide evidence that p-tau biomarkers are more closely associated with amyloid plaques than tau tangles, measured with PET.
jamanetwork.com/journals/jaman.....
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2

1

6

Ash Paul @pash22 · Dec 12, 2022

Genetic risk for attention-deficit/hyperactivity disorder predicts cognitive decline and development of Alzheimer's disease pathophysiology in cognitively unimpaired older adults
nature.com/articles/s4138... via @dtieffa et al

nature.com
Genetic risk for attention-deficit/hyperactivity di
Molecular Psychiatry - Genetic risk for
attention-deficit/hyperactivity disorder predic...

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Lon S. Schneider, MD @LonSchneiderMD · Dec 12, 2022

Ho hum, so this ADHD polygenic risk score is misspecified, possibly overweighting items associated with cognitive function.
On the other hand, just to be safe, "All I want for Christmas is ... is... a box of Addies?"

ADNI, The gift that keeps on giving 🎁.

Merry Christmas 🎄🇺🇸

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Ash Paul @pash22 · Dec 19, 2022

New commentary in @bmj_latest by Seb @seb_walsh et al on Lecanemab 📄

Seb Walsh @seb_walsh · Dec 19, 2022

Replying to @seb_walsh

Hyperbolic rhetoric is cruel on patients/families, and problematic for clinicians and health systems.

Co-authors: @r_merrick Shirley Nurrock, Edo Richard, and Caro...
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1

1

13

2.4K

Ash Paul @pash22 · Dec 21, 2022

New @newsweek article on Lecanemab by @95gunn & highlighted by Madhav @MadhavThambiset

Madhav Thambisetty @MadhavThambiset · Dec 21, 2022

"The drug has significant risks, including bleeding & brain swelling. Fiaci estimates the annual price of treatment would be

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@newsweek · Dec 21, 2022
New [@newsweek](#) article on Lecanemab by [@yagunn](#) & highlighted by Madhav [@MadhavThambiset](#)

Madhav Thambisetty [@MadhavThambiset](#) · Dec 21, 2022
"The drug has significant risks, including bleeding & brain swelling. Eisai estimates the annual price of treatment would be somewhere between \$9,249 & \$35,605 & the drug has only a modest effect on the debilitating progress of Alzheimer's"
[@ProfRobHoward](#) [@pash22](#) [@gregggonssalves](#) ...
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1

1

7

2.5K

barttels [@barttels2](#) · Dec 21, 2022
This just in (yesterday actually).

They haven't given up, though [#Aduhelm](#) still looks like a stop, and you'll get run over if you stand in the way of lecanemab.

endpts.com
Ahead of lecanemab decision, Alzheimer's group: Aduhelm's successor is now weeks away from its PDUFA date — and several advocacy group...

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4

1.5K

Robert Howard [@ProfRobHoward](#) · Dec 21, 2022
At the end of all the scrambling for regulatory approvals and reimbursement, no sensible or responsible physician is going to prescribe this for their patients. It's a denial of reality to pretend otherwise. Clinical sense will prevail. We need to keep looking for effective Rx.

3

3

18

5.6K

Madhav Thambisetty [@MadhavThambiset](#) · Dec 22, 2022
I think making "Did no harm to patient" a billable procedure for physicians would represent a paradigm-shifting advance in care for [#Alzheimers](#) patients.

4

5

13

5.6K

Jason Cohen [@MemoryDoc](#) · Dec 22, 2022
🔥🔥
That's going to need some silvadene

1

1

982

Ash Paul [@pash22](#) · Dec 28, 2022
Highlighted by [@barttels2](#) , here's a new article by [@kanokomatsuyama](#)
"Blood Tests for Alzheimer's Are the Next Big Focus for Japan's [@FujirebioUS](#) "

bloomberg.com
Blood Tests for Alzheimer's Are the Next Big Focus for Japan's
A tiny Tokyo-based diagnostics firm that developed the first US-approved spinal fluid ...

2

2

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1K

barttels [@barttels2](#) · Dec 28, 2022
With no enthusiasm!

barttels [@barttels2](#) · Dec 28, 2022
Replying to [@phsiao4](#)
"Convenient testing will also help physicians decide who's qualified to receive lecanemab, the first-ever therapy to clearly

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barttels @barttels · Dec 28, 2022

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"Convenient testing will also help physicians decide who's qualified to receive lecanemab, the first-ever therapy to clearly slow the progress of Alzheimer's."

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1 1 1.6K

**barttels** @barttels2 · Dec 28, 2022

Replying to @barttels2 and @phsiao4

"It's really important for us that blood tests become a standard for diagnosing Alzheimer's disease and are commonly used. Once we establish what we can do, we'll supply ingredients to other companies to swiftly create and expand the market." ...

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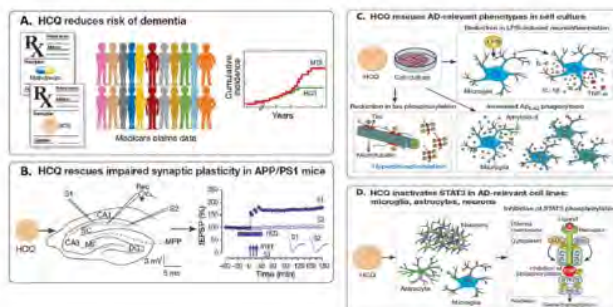
1 1 1.6K

**Ash Paul** @pash22 · Dec 28, 2022

Very early days yet but new hopes raised on HCQ Rx for AD from Madhav @MadhavThambiset

Madhav Thambisetty @MadhavThambiset · Dec 28, 2022

'HCQ lowers Alzheimer's risk & rescues molecular phenotypes related to AD'. With real world clinical data & experimental validation in cell culture & a transgenic model we show that HCQ is a plausible disease modifying Rx tinyurl.com/yfkhbpn5 @ProfRobHoward @pash22 @EricTopol



3 1 3 1.9K

**Robert Howard** @ProfRobHoward · Dec 28, 2022

Hope for mice, at least.

3 5 1.2K

**Madhav Thambisetty** @MadhavThambiset · Dec 28, 2022

And men too Rob! Among 109,124 RA patients from routine clinical care, HCQ initiation was associated with a lower risk of incident AD compared to methotrexate initiation across 4 alternative analyses schemes addressing specific types of biases.

2 5 1.1K

**Robert Howard** @ProfRobHoward · Dec 28, 2022

Let's see the phase 2/3 RCT! Happy to do it in the NHS if you are interested.

1 3 1.1K

**Jan** @810964733763B

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Robert Howard @ProfRobHoward · Dec 28, 2022
Let's see the phase 2/3 RCT! Happy to do it in the NHS if you are interested.

Madhav Thambisetty @MadhavThambiset · Dec 28, 2022
I would love to take you up on this offer. Absolutely. We discuss in the paper a prior small negative trial as well and reasons why we think a better designed trial is worth doing today.

Ash Paul @pash22 · Dec 29, 2022
HT @barttels2
"Seeking maximum profits, @biogen set an 'unjustifiably high price' for Alzheimer's treatment, US @congressdotgov investigation finds" statnews.com/2022/12/29/8-k... via @rachelcohrs & @adamfeuerstein & @damiangarde



From statnews.com

Ash Paul @pash22 · Dec 29, 2022
The link to the full @OversightDems & @EnergyCommerce report is given in the above article mobidrive.com/sharelink/p/cG...



barttels @barttels2 · Dec 29, 2022
Ceding this little endeavor to a far better person than I

Ali Ezzati @AE_MD · Dec 29, 2022
This is 46p. Anyone cares to provide a twittorial, please! & is this just a report, or its going to lead to change? I'm not interested in congressional reports with no action as a tax payer, nor as a doctor!

Madhav Thambisetty @MadhavThambiset · Dec 29, 2022
Every page is worth a read. I'm amazed at how precise the language

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- Adrian H** @Adrian_H
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nor as a doctor!

31.1K

...

Madhav Thambisetty @MadhavThambiset · Dec 29, 2022 ...

Every page is worth a read. I'm amazed at how precise the language is & the forensic level of detail. Who actually writes these reports @PamBelluck @adamfeuerstein @rickberke? The scientific nous here is impressive. Are there scientists on the committee or staff?

31.1K

...

Jean C9orf72 @jeanc9orf72 · Dec 29, 2022 ...

This celebration of a Jonathan swiftian proposal from congress re: people with Alzheimer's is so disturbing. We have on record, congress declaring no Alzheimer's drug that costs 56k will ever be just , regardless of what it can do. It's horrifying.

21K

...

David Rind @dmrind · Dec 30, 2022 ...

Does the report really say that an Alzheimer's drug could never be worth \$56K per year? I didn't see that, but it's a long report...

2975

...

Jean C9orf72 @jeanc9orf72 · Dec 30, 2022 ...

Congress gleefully reports,with help from credulous reporters, that wide adoption of Aduhelm would have harmed Medicare. They do not couch this in cost benefit terms. It's absolute. Anything costing Medicare so much must be bad.

21K

...

barttels @barttels2 · Dec 30, 2022 ...

If something is not effective, by definition it can't be cost effective.

11.1K

...

Jean C9orf72 @jeanc9orf72 · Dec 30, 2022 ...

See you are confused, which is reasonable given the abysmal reporting. There was never an assertion of clinical efficacy.

1972

...

barttels @barttels2 · Dec 30, 2022 ...

Yes there was.

1K

...

Ash Paul @pash22 · Dec 30, 2022 ...

Yup, u are spot on. Biogen tweaked Alzheimer's phase 3 trial in 2018, sparking a stock slide fiercebitech.com/biotech/biogen... via @FierceBiotech & #NickPaulTaylor

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1 1 3 1K

barttels @barttels2 · Dec 30, 2022
For some reason, probably my mother's miserable trajectory with Alzheimer's, I paid a lot of attention to this from the beginning

I'd be sympathetic to any potential sufferer screaming for someone to pay for anything

But why should so many pay for effectively nothing?
1 1 8 1K

Ash Paul @pash22 · Jan 3, 2023
HT @barttels : Kasper @kasperkleppe & many other authors in this tagged group @StefanoSensi14, @KasperBJohnsen, @KarlHerrup, @geoperry & @AlbertoEspay have written article on #Clarity trial & drawn attentn of @US_FDA to Lecanemab trial's drawbacks

Kasper Planeta Kepp @KasperKepp · Jan 3, 2023
The anti-amyloid monoclonal antibody Lecanemab: 16 cautionary notes with @StefanoSensi14 @KasperBJohnsen Jorge Barrio, Poul Høilund-Carlson, Rachael Neve, Abass Alavi, @KarlHerrup @geoperry Nikolaos Robakis, Bryce Vissel, @AlbertoEspay ...
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Abstract
The recent CLARITY AD results for the monoclonal anti-amyloid antibody Lecanemab have been interpreted as promising, supporting the amyloid hypothesis of Alzheimer's disease and leading to consideration for approval by the Food and Drug Administration. Here we explain why the claimed benefits on cognition and activities of daily living are uncertain, why Lecanemab may yield net harm for some subsets of patients and why the data do not prove the amyloid hypothesis but support other important population covariates driving disease. We note potential biases in the cohort arising from inclusion bias, unblinding, and dropouts, among other issues, which may affect the veracity of the data. Together with substantial adverse effects and subgroup heterogeneity, we conclude that Lecanemab's efficacy is not clinically meaningful and may be insignificant when considering the study limitations and biases highlighted. The data are consistent with numerous analyses to date suggesting that Aβ and its derivatives are not the main causative agents of Alzheimer's dementia.
Keywords: Alzheimer's disease; beta-amyloid; antibody; Lecanemab; subgroup analysis

2 5 10 4.5K

barttels @barttels2 · Jan 4, 2023
Thanks, Ash. It's an outstanding piece. I hope everyone will read through at least some of it.

Really only 10 pages (second 10 are references).

They did not phone this in; appears very well thought through and documented.

1 1 7 1K

Ash Paul @pash22 · Jan 4, 2023
Very sorry for the typo, the lead author is @KasperKepp and NOT @kasperkleppe

Relevant people

- Adrian H**
@Adrian_H
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- Ash Paul** @pash22 · Jan 4, 2023
Very sorry for the typo, the lead author is [@KasperKepp](#) and NOT [@kasperkleppe](#)
- David Rind** @dmrind · Jan 4, 2023
I'm not sure the number of dropouts for AEs is correct in this: 6.9% vs 2.9% is the number of discontinuations for AEs, but dropouts for AEs seems to have been 5.7% vs 3.1%. Also not sure I understand the concern about figure S6. Isn't this just censoring after an event?
- barttels** @barttels2 · Jan 4, 2023
Hopefully your questions will be answered.
- Ash Paul** @pash22 · Jan 4, 2023
New article by Zach [@ZacharyBrennan](#) on [@congressdotgov](#) inquiry into 'highly atypical' [@US_FDA](#)-[@biogen](#) ties that ended with a damning report, but no repercussions
- 
Congressional inquiry into 'highly atypical' FDA-Biogen ties ends with da...
From endpts.com
- barttels** @barttels2 · Jan 4, 2023
"Congressional committees ... called on the FDA to 'take swift action to ensure its processes for reviewing future Alzheimer's disease treatments do not lead to the same doubts about the integrity of FDA's review.'"
What integrity?
1 1 4 1.3K
- Ash Paul** @pash22 · Jan 4, 2023
Will [@US_FDA](#) take expedited action before the Lecanemab Cttee hearing in a few days time?
1 1 4 1.3K
- barttels** @barttels2 · Jan 4, 2023
Calls for a resounding chorus of
"Sure, Jan." 🙄
1 1 3 1.2K
- Ash Paul** @pash22 · Jan 4, 2023
Madhav [@MadhavThambiset](#)'s tweet on [@NEJM](#) paper by [@DrNikorasu](#) et al
"Multiple Cerebral Hemorrhages in a Patient Receiving Lecanemab and Treated with t-PA for Stroke"
[nejm.org/doi/full/10.10...](#)

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I know what I'd wish.
And how I'd bet.
(They're not the same)

2 1 2 1.4K



Ash Paul @pash22 · Jan 5, 2023
Madhav @MadhavThambiset in twitter conversation with Brian @BrianSkorney abt Lecanemab



Madhav Thambisetty @MadhavThambiset · Jan 5, 2023
Replying to @BrianSkorney
Not sure it is as simple. Routine APOE genotyping of cognitively impaired Alzheimer's patients to guide clinical decision making is entirely uncharted territory. It presents multiple legal & ethical challenges & will be an unprecedented societal challenge ...
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1 2 5 3.2K



Ash Paul @pash22 · Jan 6, 2023
Tweeetorial by Matthew @schrag_matthew on @alzassociation aggressively promoting the Lecanemab agenda to @US_FDA



Matthew Schrag @schrag_matthew · Jan 5, 2023
The Alzheimer's Association wants you to believe there is a "consensus" that Biogen/Eisai's drug Lecanemab is a breakthrough. They are circulating a letter signed by ~200 physicians/scientists to support this claim. BUT - most work for/with Biogen/Eisai. alz.org/media/Document...

2 1 11 3.1K



Stefano L. Sensi @StefanoSensi14 · Jan 6, 2023
some levels of critical thinking finally surfacing in major venues



science.org
Lecanemab's Rough Progress
Lecanemab's Rough Progress

3 2 13 3.6K



barttels @barttels2 · Jan 6, 2023
Oh it has been. Add this to the list of great pieces ~~ comments, too (one sorry exception).

Thanks!

1 3 745



Ash Paul @pash22 · Jan 8, 2023
Someone asked a Q abt association btwn insurance and MCI in USA. Here's Scott @LTCShop 's answer



LTCShop.com @LTCShop · Jan 7, 2023
Replying to @barttels2 @ideapharma and @pash22
Zero chance of buying long-term care insurance if there are any signs of a mild cognitive impairment. A policy must be purchased long before any signs of cognitive decline.

1 3 990



Ash Paul @pash22 · Jan 8, 2023
Commenting on a recent story by @H_M_MAC, here's Jeff @Jeff_BrownDuke's prediction on the future of Lecanemab after its'



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Ash Paul @pash22 · Jan 8, 2023
Commenting on a recent story by @H_M_MAC , here's Jeff @Jeff_Browndyke 's prediction on the future of Lecanemab after its' approval by @US_FDA.

Jeff Browndyke @Jeff_Browndyke · Jan 6, 2023
Replying to @a_charidimou and @schrag_matthew
Prediction: More deaths will prompt serious questions, outcry and possibly FDA to reconsider. biospace.com/article/third-...
1 4 990

Ash Paul @pash22 · Jan 8, 2023
Here's Jean @jcl_lambert 's tweet on Lecanemab

Jean-Charles Lambert @jcl_lambert · Jan 7, 2023
Huge doubt: the more I look at the data and read the comments on lecanemab, the more I have the impression that it could be an indirect (passive?) effect not necessarily linked to the amyloid cascade hypothesis..
2 4 1.1K

Timothy Daly, PhD @PhilAlz · Feb 1, 2023
May interest members of this thread:

Timothy Daly, PhD @PhilAlz · Feb 1, 2023
@bmj_latest published my letter on @seb_walsh et al.'s editorial on lecanemab. I defend the principle of truthfulness in dementia research & communication to protect against hype and false hope. We must stay data-focused regarding treatment expectations. ...
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1 6 996

Timothy Daly, PhD @PhilAlz · Feb 2, 2023
May interest members of this thread:

Timothy Daly, PhD @PhilAlz · Feb 2, 2023
In @LancetLongevity I consider what "revolution" means in Alzheimer's research, the ethics of AD biomarkers, and the need to avoid over-reliance on the amyloid-lowering strategy.
[thelancet.com/journals/lanhl...](#)
1 3 956

Ash Paul @pash22 · Feb 2, 2023
Validity and Performance of Blood Biomarkers for Alzheimer Disease to Predict Dementia Risk in a Large Clinic-Based Cohort
[n.neurology.org/content/100/5/...](#) via @VincentPlanche et al

neurology.org
Validity and Performance of Blood Biomarkers fo
Background and ObjectiveBlood biomarkers for
Alzheimer disease (AD) have consistently ...
2 1 5 718

barttels @barttels2 · Feb 2, 2023
Seems closer to verification than prediction, or a bit of both

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@Adrian_H
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Association of Phosphorylated Tau Biomarkers With Amyloid PET vs Tau ...

From jamanetwork.com

3 3 635

Joseph Therriault @JosephTherr · Feb 5, 2023

Bonjour Nicholas, 100% correct!
The associations with tau-PET are still quite strong (as can be seen clearly in the figures). However, p-tau is statistically more closely associated with amyloid-PET, especially in CU

1 3 583

Ash Paul @pash22 · Feb 5, 2023

Discriminative accuracy of the A/T/N scheme to identify cognitive impairment due to Alzheimer's disease [alz-journals.onlinelibrary.wiley.com/doi/10.1002/da...](#) via @JosephTherr et al

Diagnosis, Assessment & Disease Monitoring

alz-journals.onlinelibrary.wiley.com
Discriminative accuracy of the A/T/N scheme to Introduction The optimal combination of amyloid-β/tau/neurodegeneration (A/T/N) ...

2 2 602

Ash Paul @pash22 · Feb 6, 2023

'Smooth and very much on track': @EisaiUS reports first shipments of Leqembi [endpts.com/smooth-and-ver...](#) via @Nicole_DeFeudis

endpts.com
'Smooth and very much on track': Eisai reports f Eisai and Biogen began shipping out doses of their newly approved Alzheimer's drug Leqem...

1 1 4 1.2K

barttels @barttels2 · Feb 6, 2023

"In the US, if the FDA grants priority review to our supplemental BLA application, we could receive full traditional approval & broader coverage from CMS in the summer of this year, just several months away."

Yup, called this one from the beginning.

Handwriting on the wall.

2 1 575

Ash Paul @pash22 · Feb 7, 2023

Experts temper hope for new FDA-approved Alzheimer's drug [theglobeandmail.com/canada/article...](#) via @wencyleung

theglobeandmail.com
Experts temper hope for new FDA-approved AlzI Lecanemab, marketed under the brand name Leqembi, is the second Alzheimer's drug to ...

2 2 634

Stefano L. Sensi @StefanoSensi14 · Feb 8, 2023

going down quickly- good riddance!

forbes.com

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Stefano L. Sensi @StefanoSensi14 · Feb 8, 2023
going down quickly- good riddance!

forbes.com
The Scandal Of Alzheimer's
Appallingly, for decades Alzheimer's researchers have pursued a dead-end ...

1

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628

Ash Paul @pash22 · Feb 12, 2023
Madhav @MadhavThambiset raises an imp point abt financial toxicity and Alz Rx

Madhav Thambisetty @MadhavThambiset · Feb 12, 2023
1/n This is an issue that is going to become even more relevant & complex as we begin testing experimental #Alzheimers treatments at preclinical stages of the disease ie in people WITHOUT any memory impairment. @bethpinsker writes here that "The only real option for help to pay x.com/LEAD_Coalition...

1

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4

2.4K

Ash Paul @pash22 · Feb 15, 2023
Health experts want @US_FDA safety review of fast-tracked Alzheimer's drug Lecanemab [axios.com/2023/02/06/fda...](https://www.axios.com/2023/02/06/fda...) via @OrianaBeLike

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2

641

From axios.com

Nicolas Villain @nvillain_alz · Feb 15, 2023
Thx @pash22
Can anyone explain to me what is "Doctors for America", the experts mentioned in this article?

doctorsforamerica.org
PRESS RELEASE: Doctors For America's FDA Tasl
FOR IMMEDIATE RELEASE Doctors for America
PO Box 53313 1921 Florida Ave NW ...

1

1

533

Ash Paul @pash22 · Feb 15, 2023
Hi Nicolas, chk them out at [@drsforamerica](https://www.doctorsforamerica.org) .
[doctorsforamerica.org](https://www.doctorsforamerica.org)
The head of this NGO is @Angie_Bakke

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From doctorsforamerica.org

1 2 678

Ash Paul @pash22 · Feb 16, 2023
Drug trial 4 Alz disease is a game changer: An antibody Rx reduces measurements of brain abnormalities called amyloid plaques in people w/ Alz & ↓ clin decline. This will help in developing Rx to treat & prevent Alz [nature.com/articles/d4158...](https://www.nature.com/articles/d4158...) via @BannerAlzheimer 's #EricReiman

nature.com

Drug trial for Alzheimer's disease is a game cha

Nature - Clinical trial of an antibody against amyloid-β meets with success.

1 1 1 657

barttels @barttels2 · Feb 16, 2023
"Gamechanger?" C'mon



From endpts.com

2 2 692

Ash Paul @pash22 · Feb 17, 2023
'It's night and day': Biogen's new Alzheimer's drug Lecanemab may spur more investment in fighting the disease [bostonglobe.com/2023/02/15/bus...](https://www.bostonglobe.com/2023/02/15/bus...) via @RLCscienceboss

bostonglobe.com

'It's night and day': Biogen's new Alzheimer's dr

Since Leqembi is far from a cure, doctors and drug developers are already thinking about h...

2 2 643

barttels @barttels2 · Feb 17, 2023
I leave this more measured piece open on my browser for a reason. [@schrage_matthew](#)



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barttels @barttels2 · Feb 17, 2023
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From endpts.com

1 1 606



Ash Paul @pash22 · Feb 17, 2023
Internal review found 'falsified data' in [@Stanford](#) President's Alzheimer's research, colleagues allege
[stanforddaily.com/2023/02/17/int... via @tab_delete](#)

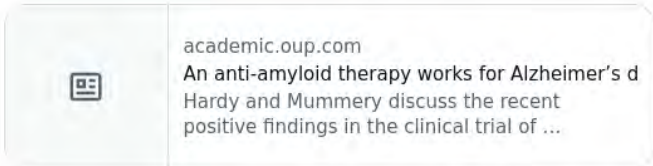


From stanforddaily.com

1 3 9 1.3K



Ash Paul @pash22 · Feb 18, 2023
An anti-amyloid therapy works for Alzheimer's disease: why has it taken so long and what is next? [academic.oup.com/brain/advance-...](#) via [@cathmummery](#) et al



1 1 1 663



barttels @barttels2 · Feb 19, 2023
🤔

1 1 715



Ash Paul @pash22 · Feb 19, 2023
Could Alzheimer's be caused by an infection?
[theguardian.com/society/2023/f... via @drdavidcox](#)



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From theguardian.com

1 2 4 721



Madhav Thambisetty @MadhavThambiset · Feb 19, 2023 ...

We showed in this paper that several immune regulatory proteins involved in anti viral host defense & cytokine signaling are up regulated in young APOE4 brains and down in AD brains

[@JacksonARoberts](#)



From pubmed.ncbi.nlm.nih.gov

1 1 5 812



Alberto J Espay @AlbertoEspay · Feb 19, 2023 ...

1. The infection-AD connection is well established. 2. AD is a syndrome (e.g., HSV-1 is etiological in one small subtype, not in everyone). 3. Infectious exposures catalyze the nucleation of Aβ42 into amyloid, depleting the former.



1 2 3 731



Alberto J Espay @AlbertoEspay · Feb 19, 2023 ...

This is [@Kariem_Ezzat](#)'s post on this preprint.



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1.1K

Ash Paul @pash22 · Feb 21, 2023

@US_FDA adds warning of 'larger areas of bleeding' in brain to Biogen's Aduhelm label
[endpts.com/fda-adds-wami...](#) via @ZacharyBrennan @AE_MD @a_charldimou

endpts.com
Updated: FDA adds warning of 'larger areas of b
The FDA last week signed off on a safety-
related change to the label of Biogen's ...

2

7

671

Timothy Daly, PhD @PhilAlz · Feb 22, 2023

Our recent book chapter may interest members of this thread ([twitter.com/PhilAlz/status...](#)). DM me for PDF.

Timothy Daly, PhD @PhilAlz · Feb 22, 2023

1/5 with @AlbertoEspay & @KarlHerrup in @ELSNeurology Handb Clin Neurol Ch. 10 we argue research into neurodegeneration has not followed Popper's a priori "conjectures and refutations." Saving the amyloid hyp has meant: post hoc modifications...
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1.5K

Ash Paul @pash22 · Feb 22, 2023

Apparently, Popper's a priori has many detractors also. "Popper and Wittgenstein on the Metaphysics of Experience" [link.springer.com/article/10.100...](#) via @MaastrichtU 's #HarrySmit

link.springer.com
Popper and Wittgenstein on the Metaphysics of I
Journal for General Philosophy of Science - In
the Tractatus Wittgenstein argued that there ...

2

5

710

Timothy Daly, PhD @PhilAlz · Feb 22, 2023

It certainly does, and is no perfect worldview. However, for AD research, where we've just kept going with the same idea for decades based on data from familial AD and a very short, elegant paper written on it in 1992, perhaps a sprinkle of Popperian thinking would be useful.

2

4

705

Ash Paul @pash22 · Feb 23, 2023

Tweet from Alexander @Alexander_Tin on @CMSGov response to @alzassociation HT @barttels2

Alexander Tin @Alexander_Tin · Feb 22, 2023

From @CMSGov's release on response today to @alzassociation re: covering amyloid Alzheimer's treatments

"as of the date of this letter, there is not yet evidence meeting the criteria for reconsideration"

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Alexander Tin @Alexander_Tin · Feb 22, 2023
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"as of the date of this letter, there is not yet evidence meeting the criteria for reconsideration"...
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The Centers for Medicare & Medicaid Services (CMS) is committed to helping people get timely access to treatments and improving care for people with Alzheimer's disease and their families.
At this time, CMS is not reconsidering the national coverage determination (NCD) for Food and Drug Administration (FDA)-approved monoclonal antibodies directed against amyloid for the treatment of Alzheimer's disease. We recognize that these medications are a unique, new class of drugs, and we regret that the decision could not be more favorable.
After careful review of the request and supporting documentation, we are making this decision because, as of the date of this letter, there is not yet evidence meeting the criteria for reconsideration. CMS's letter to the Alzheimer's Association outlines the key questions that need to be addressed for reconsideration. As defined in statute, to provide coverage nationally, CMS is required to examine whether a medication is reasonable and necessary. This standard differs from the criteria used by the FDA to assess whether medications are safe and effective. We are aware that additional publications may be forthcoming that include information relevant to the questions included in the current NCD. CMS will expeditiously review any new evidence that

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7

1.1K

Ash Paul @pash22 · Feb 23, 2023
A 19-year-old is the youngest person to be diagnosed with Alzheimer's disease: the cause is a mystery theconversation.com/a-19-year-old-... via @shabir_osman

A 19-year-old is the youngest person to be diagnosed with Alzheimer's ...

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761

barttels @barttels2 · Feb 23, 2023
This is bizarre.
Not to be morbid, but hopefully his brain will be donated to science someday.

1

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738

Ash Paul @pash22 · Feb 23, 2023
US @MedicareGov says no change to Alzheimer's drug restrictions reuters.com/business/healthcare-pharmaceuticals/us-medicare-says-no-change-to-alzheimers-drug-restrictions via @reutersDeenaB

U.S. Medicare says no change to Alzheimer's drug restrictions

1

3

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6.9K

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U.S. Medicare says no change to Alzheimer's drug restrictions

From reuters.com

1 3 7 6.9K

**Caregiver** @stevecripe57 · Feb 23, 2023

If I was told I had early Alzheimer's, I would want the drug. What's the alternative? It can't be any worse than a slow death and not remembering anyone.

2 2 1 821

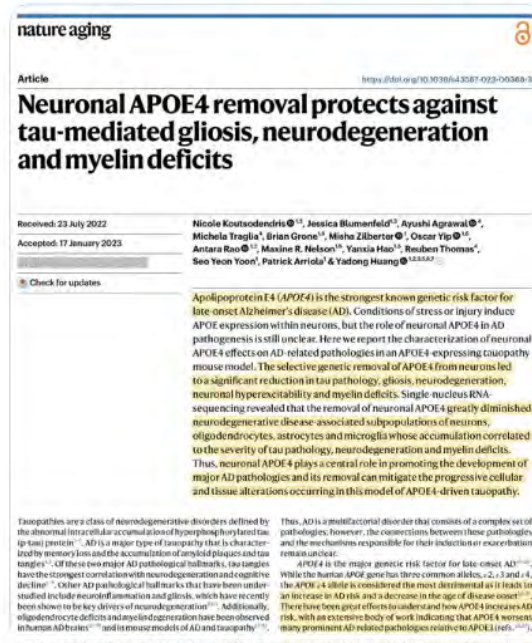
**barttels** @barttels2 · Feb 23, 2023

On an 18-pt scale, the difference in decline between leqembi and placebo was .45 at 18 months. It doesn't give anyone memory back. Known hazards as well.

1 1 3 772

**Ash Paul** @pash22 · Feb 23, 2023

Neuronal APOE4 removal protects against tau-mediated gliosis, neurodegeneration and myelin deficits in mice
[nature.com/articles/s4358...](https://doi.org/10.1016/j.neuron.2023.02.008) via @GladstoneInst researchers



1 1 3 782

**Ash Paul** @pash22 · Feb 27, 2023

@US_FDA's #BillyDunn of Aduhelm fame to leave the agency immediately
[statnews.com/2023/02/27/fda...](https://www.statnews.com/2023/02/27/fda-billy-dunn/) via @adamfeuerstein & @damiangarde



From statnews.com

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From statnews.com

3 2 4 1K

LogarithmicDis @LogarithmicDis · Feb 28, 2023

Worse, the Cavazonni era still remains. She's his superior.

[forbes.com/sites/davidgor...](#)

1 2 3 1.4K

barttels @barttels2 · Feb 28, 2023

Author is not on Twitter. But if you put his name into the search box, you'll learn a lot.

1 567

Ash Paul @pash22 · Feb 28, 2023

Yes he is. His twitter account is [@GortlerDavid](#), albeit it is a passive account

[business.catholic.edu/faculty-and-re...](#)

1 1 588

barttels @barttels2 · Feb 28, 2023

obie @MJOBIE7 · Jan 13, 2023

U.S. Senate Hearing
Dr. David Gortler
Former Senior Advisor
FDA
...
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1 1 1.2K

Ash Paul @pash22 · Feb 28, 2023

Wall Street is very worried at [#BillyDunn](#) 's departure from [@US_FDA](#), according to [@damiangarde](#)

Amylyx Pharmaceuticals, maker of a novel treatment for ALS, and Sarepta Therapeutics, at work on a gene therapy for Duchenne muscular dystrophy, declined by as much as 5%.

The share prices of multiple neuroscience-focused biotech companies tumbled yesterday on the news that Dunn, perceived as an industry-friendly regulator, would no longer be in charge of

The fear is that the "loss of a more permissive, industry-friendly voice is a long-term negative" for neuroscience

2 8 959

barttels @barttels2 · Feb 28, 2023

Wow!

If that doesn't say it all, it says a lot!

1 759

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Ash Paul @pash22 · Mar 1, 2023

New questions raised by Madhav [@MadhavThambiset](#) on Neurofilament Light (NfL)

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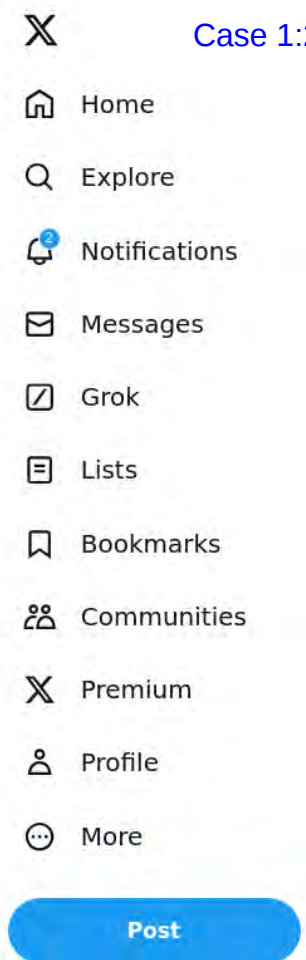
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Ash Paul @pash22 · Mar 1, 2023
New questions raised by Madhav @MadhavThambiset on Neurofilament Light (NFL)

Madhav Thambisetty @MadhavThambiset · Mar 1, 2023
1/n Thoughts on Neurofilament Light (NFL) as a neurodegeneration biomarker. I expect to hear a lot on it in the upcoming #Tofersen Adcom. @US_FDA refers to it as a promising biomarker of neurodegeneration in several diseases at the Relyvrio #ALS approval 🌟 @ProfRobHoward @pash22

As I mentioned, it's being studied in many different neurologic diseases, particularly the neurodegenerative diseases. I think that there are some data that show in a variety of different diseases that levels are elevated and may track with the disease course. It is being examined as a biomarker in a number of studies. It is not yet at a point where we would -- we still consider it exploratory, but we do see it as a promising biomarker.

So it is being included in a lot of studies with the idea that if there is a reduction in neurofilament levels, that that would be suggestive of an effect on the slowing or reducing the degeneration being seen in the disease.

I think, as I mentioned, we're at the point now where we see this as a promising biomarker, but we still see it as an exploratory biomarker, and we're hoping to continue to collect more data on it to see how useful it will be in clinical trials

Ash Paul @pash22 · Mar 1, 2023
US @icer_review Publishes Evid Report on Lecanemab for Alz' Disease.
Evid is rated as promising but inconclusive to determine whether lecanemab provides a net health benefit over supportive care; it shud b priced between \$8,900 - \$21,500 per year
icer.org/wp-content/upl...

Ash Paul @pash22 · Mar 1, 2023
New head of @US_FDA 's neuroscience office #TeresaBuracchio takes over at crucial time statnews.com/2023/02/28/new... via @adamfeuerstein & @john_wilkerson

statnews.com
New head of FDA's neuroscience office takes over
The new head of the FDA's Office of Neuroscience is stepping into an increasingly ...

Timothy Daly, PhD @PhilAlz · Mar 3, 2023
May interest members of this thread:

Timothy Daly, PhD @PhilAlz · Mar 3, 2023
In @SpringerNature Neurological Sciences I describe the harms of four kinds of misuse of scientific language in neurodegeneration research: "biomarker of disease" substitution

Relevant people

Adrian H @Adrian_H
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May interest members of this thread:

Timothy Daly, PhD

@PhilAlz · Mar 3, 2023

In @SpringerNature Neurological Sciences I describe the harms of four kinds of misuse of scientific language in neurodegeneration research: "tortured phrases," falsification, overstatement, and misleading use of causal language -> misunderstanding & waste. researchgate.net/publication/36...

Table 1 Harms associated with misuse of scientific language in neurodegeneration research, with examples from Parkinson's Disease and Alzheimer's Disease

Language misuse	Example	Harms associated
Tortured phrases	The nomenclatural misrepresentation of Parkinson's disease [1]	• Promotes misunderstanding of the disease entity
Falsification	Sylvain Lesné's potential fabrication of the toxicity of the Aβ ²⁵⁶ oligomer in Alzheimer's Disease [2]	• Promotes misunderstanding of the disease entity • Leads to waste of research resources
Therapeutic overstatement	Metabolic enhancement protocols of Alzheimer's Disease [3] promoted in scientific articles, the lay press, and for-profit books based on individual case studies without any kind of control group	• Promotes false hope • Promotes misunderstanding of the disease entity • Causes financial harm • Undermines informed consent • Slows down research
Misuse of causal language	The "contributions" of PET amyloid scan to improved outcomes in Alzheimer's Disease [4]	• Promotes false hope • Promotes misunderstanding of the disease entity • Slows down research

1 3 1.2K

Ash Paul

@pash22 · Mar 3, 2023

@LonSchneiderMD & @schrug_matthew are quoted in this @NeuroAdvisor article mentioned by @MadhavThambiset on 'Forecasting Real-World Usage of Lecanemab for AD Treatment: An Expert Roundtable' [↓](#)

Madhav Thambisetty

@MadhavThambiset · Mar 3, 2023

"potential for 3 deaths associated with #lecanemab could foreshadow what would be in real-world circumstances & suggest that rate could be 3 per<1700. In clinical practice it would mean that if 100K were Rx there would be 100-200 deaths" tinyurl.com/up89dw3t @ProfRobHoward

1 4 1.3K

LogarithmicDis

@LogarithmicDis · Mar 3, 2023

That risk is likely higher, due to poly pharmacy, especially blood thinners, in the elderly.

Can you imagine your loved one being Code Stroke and getting tPA?

1 2 697

Jason Cohen

@MemoryDoc · Mar 3, 2023

We've talked to our stroke team about changing tPA / TNK screening protocols. Anyone else doing this? Between the increased risks of tPA and decreased probability of benefit if ARIA is mistaken for stroke, this is problematic

5 4 756

LogarithmicDis

@LogarithmicDis · Mar 3, 2023

It's already happened:
tPA given to a #stroke patient on #lecanumab



nejm.org

Multiple Cerebral Hemorrhages in a Patient Rece

A patient with mild cognitive impairment who was treated in the extension phase of a trial o...

1 3 702

Ash Paul

@pash22 · Mar 5, 2023

US @MedicareGov just crushed the hopes of 750,000 Alzheimer's patients a year marketwatch.com/story/medicare... via @BrettArends



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US @MedicareGov just crushed the hopes of 750,000 Alzheimer's patients a year [marketwatch.com/story/medicare...](https://www.marketwatch.com/story/medicare-just-crushed-the-hopes-of-750-000-alzheimers-patients-a-year) via @BrettArends

From marketwatch.com

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907

barttels @barttels2 · Mar 5, 2023

Good grief.

"Easy demagoguery" indeed, from a finance guy/former McKinsey analyst.

As if Leqembi wasn't marginal enough on its face, has NOTHING to do with the Bruce Willis diagnosis!!

Wholesale rubbish he's trying to mass-market.

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946

Ash Paul @pash22 · Mar 6, 2023

July decision D-date set for full approval of Eisai's Alzheimer's drug, with an #ADCOM coming too endpts.com/july-decision-... via @ZacharyBrennan

endpts.com
July decision date set for full approval of Eisai's / The last time the FDA held an advisory committee meeting for an Alzheimer's drug, ...

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728

barttels @barttels2 · Mar 6, 2023

"This time [contra Aduhelm] with Eisai and Biogen's Leqembi (lecanemab), the agency will look to clear that tenuous air, and show that amyloid-lowering drugs can provide clinical benefits."

If anyone wants to bet against this getting approval, I'll take your money.

1

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1.3K

Ash Paul @pash22 · Mar 6, 2023

What happens if the #ADCOM members once again refuse to toe the official @US_FDA line? There will be no #BillyDunn now to vigorously shove the drug over the finishing line.

5

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880

Lon S. Schneider, MD @LonSchneiderMD · Mar 8, 2023

@US_FDA wants to dump Ad Comm voting "as much as possible" [@statnews](https://www.statnews.com/2023/03/08/fda-ad-com-voting/) "The most important thing...is that the purpose is not to take a vote on the approval of a product," voting is "a habit, it's not a requirement, and it's not very useful....an FDA decision, not an AC decision."

1

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1.4K

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The most important thing...is that the purpose is not to take a vote on the approval of a product," voting is "a habit, it's not a requirement, and it's not very useful....an FDA decision, not an AC decision."

1 1 6 1.4K

barttels @barttels2 · Mar 8, 2023
What a sham.

Probably the only way for people outside to get a real reading on their little "chat."

1 3 679

Ash Paul @pash22 · Mar 8, 2023
Here's the rest of the Q&A answer session with [@FDACommissioner](#) [statnews.com/2023/03/07/fda...](#) via [@DrewQJoseph](#)



Q&A: Califf on obesity drugs, advisory panels, and how threats hurt recr...

From statnews.com

1 1 749

Ash Paul @pash22 · Mar 9, 2023
New paper by Kasper [@kasperkleppe](#) et al [📄](#)
"Alzheimer's disease and the amyloid hypothesis: A critical review"

Kasper Planeta Kepp @KasperKepp · Mar 9, 2023
Lots of talk about the amyloid hypothesis after Aducanumab & Lecanemab. A historic data-based discussion: "Alzheimer's disease and the amyloid hypothesis: A critical review". [zenodo.org/record/7711807](#)
(working with collaborators on a much improved version, to be... [Show more](#)

1 1 6 1.1K

Timothy Daly, PhD @PhilAlz · Mar 9, 2023
Interesting! My piece
"Learning from the amyloid hypothesis: adaptability, brevity, and clarity of ideas" was just accepted for publication. If anyone's interested DM me for the accepted manuscript.

2 4 719

Ash Paul @pash22 · Mar 10, 2023
New [@LillyPad](#) trial result and comment by Alberto [@AlbertoEspay](#) [📄](#)

Alberto J Espay @AlbertoEspay · Mar 9, 2023
Hypothesis: Aβ42 is toxic.
Task: Lowering Aβ42 levels before #Alzheimers onset.
Trial: Anti-Aβ42 prophylaxis in NORMAL people with amyloid plaques (A4 Study).
Results at 10 years: Futile.... [Show more](#)

"These findings indicate that amyloid is a key driver of cognitive decline"

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Task: Lowering A β 2 levels before Alzheimer's onset.

Trial: Anti-A β 42 prophylaxis in NORMAL people with amyloid plaques (A4 Study).
Results at 10 years: Futile....
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"These findings indicate that amyloid is a key driver of cognitive decline at the preclinical stage of Alzheimer's disease. Solanezumab did not substantially impact amyloid plaque burden in the brain, and unfortunately did not slow cognitive decline. These data suggest that we may need to be more aggressive with amyloid removal even at this very early stage of disease," said Reisa Sperling, M.D., a neurologist at the Brigham and Women's Hospital, Harvard Medical School and the A4 Study project director. "We are so very grateful to the participants, their study partners, the clinical trial site investigators and staff, and the entire study team for their longstanding dedication to this important study. It is imperative that we learn everything we can to inform ongoing and future trials in our quest to prevent memory loss due to Alzheimer's disease."

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1.2K

Lon S. Schneider, MD @LonSchneiderMD · Mar 10, 2023
Allow me to translate the presser, Reisa's quote:
"Oops, we used the wrong antibody, lecanemab or donanemab will clear plaques and show clinical benefit."

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824

Timothy Daly, PhD @PhilAlz · Mar 10, 2023
Genuinely chuckled but it's actually really sad

1

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723

barttels @barttels2 · Mar 10, 2023
Ditto

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674

Ash Paul @pash22 · Mar 10, 2023
Eisai projects \$7 Billion in sales by 2030 for new Alzheimer's drug [endpts.com/eisai-projects...](#) via [@ZacharyBrennan](#)

endpts.com

Eisai projects \$7B in sales by 2030 for new Alzheimer's drug Eisai and Biogen's newly approved Alzheimer's drug Leqembi (lecanemab) is looking to do ...

2

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5

4.4K

LogarithmicDis @LogarithmicDis · Mar 10, 2023
Very much doubt that. Will probably fell the same way aduhelm did.

People don't really want to risk brain bleeding in their loved ones, and the trials did not include subject in blood thinners - which many seniors take.

2

2

692

barttels @barttels2 · Mar 10, 2023
Factor in Califf wanting to remove the advisory committee vote!

Worth listening to him here, imo. Personally, I think he's talking out of both sides of his mouth. I also think he's serious.

overcast.fm

249: Robert Califf on how drugs get approved, p
FDA Commissioner Robert Califf joins to discuss his first year on the job, the future of drug ...

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FDA Commissioner Robert Califf joins to discuss
his first year on the job, the future of drug ...

1 1 657

Lon S. Schneider, MD @LonSchneiderMD · Mar 10, 2023 ...
Advisory committees are useful to @US_FDA (and a lot of other folk)
for cover. Anything else and they are considered rogue.

4 1 670

Ash Paul @pash22 · Mar 10, 2023 ...
"Unwanted Advice? Frequency, Characteristics, And Outcomes Of
Negative @US_FDA Advisory Committee Votes For FDA-Approved
Drugs"
healthaffairs.org/doi/10.1377/hl... via @jsross119 et al

Health Affairs JOURNAL healthaffairs.org
Unwanted Advice? Frequency, Characteristics, A
Substantial controversy arose in 2021 when the
Food and Drug Administration (FDA) approve...

1 4 6 904

Ash Paul @pash22 · Mar 10, 2023 ...
There's a v gud commentary on the above @jsross119 &
@akeselheim et al paper by @KDooleyYoung "How and when the
FDA seeks outside advice on drug approvals"

healthjournalism.org
How and when the FDA seeks outside advice on
The U.S. Food and Drug Administration could
bolster public trust in medicines through ...

3 3 8 1K

barttels @barttels2 · Mar 10, 2023 ...
Great piece, well done by @KDooleyYoung !

1 2 682


Ash Paul @pash22 · Mar 12, 2023 ...
Latest update on Biogen & Aduhelm, highlighted by Nicolas
@nvillain_alz

Allison DeAngelis @ADeAngelis_bio · Mar 12, 2023
In non-Silicon Valley Bank news, the architect of Aduhelm is
leaving Biogen.
statnews.com/2023/03/12/bio... @adamfeuerstein
@damiangarde

1 3 1.2K

Nicolas Villain @nvillain_alz · Mar 12, 2023 ...
Replying to @adamfeuerstein

Nicolas Villain @nvillain_alz · Mar 12, 2023
Replying to @adamfeuerstein



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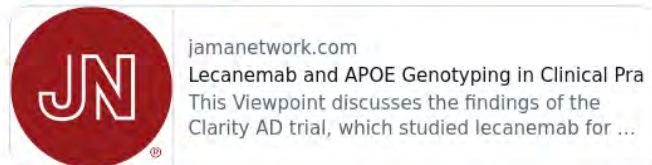
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Ash Paul @pash22 · Mar 13, 2023
Lecanemab and APOE Genotyping in Clinical Practice: Navigating Uncharted Terrain jamanetwork.com/journals/jaman... via [@MadhavThambiset](#) & [@ProfRobHoward](#)



1 2 4 816

Ash Paul @pash22 · Mar 13, 2023
US [@VeteransHealth](#) will cover the newest Alzheimer's drug statnews.com/pharmalot/2023... via [@pharmalot](#)



4 2 880

barttels @barttels2 · Mar 13, 2023



2 2 815

Jason Cohen @MemoryDoc · Mar 13, 2023
Well, that's one way to collect prospective, real-world [#lecanemab](#) data

2 2 867

barttels @barttels2 · Mar 13, 2023

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Well, that's one way to collect prospective, real-world [#lecanemab](#) data

2

2

867

barttels @barttels2 · Mar 13, 2023

Come to think of it, the VA will probably do a better job of that than random other systems.

[@eturnerm1](#) ??

2

2

817

Erick Turner @eturnerm1.bsky.so @eturnerm · Mar 14, 2023

Certainly the opportunity is there. Hopefully they'll take advantage of it and collect data in a way that is capable of answering some of the many questions that remain

1

4

953

Alberto J Espay @AlbertoEspay · Mar 15, 2023

I am mystified by the idea that "real-world" experience will answer the many questions that trials couldn't. Why bother with testing drugs in randomized, double-blind, placebo-controlled clinical trials if we can just learn all we need from trying them on (VA) patients!

2

3

8

2K

Jason Cohen @MemoryDoc · Mar 15, 2023

Can't learn everything by far, but I think we can all agree that more data from a Phase 4 would be helpful if the med will be out there anyway

2

870

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Madhav Thambisetty @MadhavThambiset · Mar 15, 2023

May be best to start with full disclosure of existing RCT results. What is the association (if any) between accelerated brain volume loss seen with [#lecanemab](#) & [#aducanumab](#) & clinical/cognitive outcomes? Does ARIA predict brain volume loss and is it associated with [NFL](#) levels?

1

2

8

2.9K

Lon S. Schneider, MD @LonSchneiderMD · Mar 15, 2023

No one's going to tell you this. They don't need to. In a decade you'll get individual patient data.

As you already see subset analyses will only raise havoc and undermine sales.

The F,D,&C Act and regulations are not about subsets.

1

2

819

Madhav Thambisetty @MadhavThambiset · Mar 15, 2023

Yet the VA formulary has already defined a "subset" to be excluded from [#lecanemab](#) ie APOE4++ carriers. It would be a reasonable hypothesis that those with higher brain volume loss are a "subset" that decline faster. An easily testable hypothesis with existing RCT data.

0:56

Exclusion Criteria

If the answer to ANY item below is met, then the patient should NOT receive lecanemab.

☐ Any medical, neurological, or mental health condition that may be a contributing/primary cause of cognitive impairment

☐ Age less than 65 years

☐ Contraindication to brain MRI

☐ Transient ischemic attack, stroke, or seizures within the past year

☐ Evidence of other clinically significant lesions on brain MRI that indicate another cause of dementia

☐ Screening MRI that shows evidence of: more than 4 microhemorrhages; a single macro hemorrhage greater than 10 mm at greatest diameter; an area of superficial siderosis; evidence of vasogenic edema; evidence of acute/subacute cerebral contusion, acute/subacute stroke, aneurysms, vascular malformations, or infective lesions; severe small vessel, or white matter disease; space occupying lesions;

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Contraindication to brain MRI

Transient ischemic attack, stroke, or seizures within the past year

Evidence of other clinically significant lesions on brain MRI that indicate another cause of dementia

Screening MRI that shows evidence of: more than 4 microhemorrhages; a single macro hemorrhage greater than 10 mm at greatest diameter; an area of superficial siderosis; evidence of vasogenic edema; evidence of acute/subacute cerebral contusion, acute/subacute stroke, aneurysms, vascular malformations, or infective lesions; severe small vessel, or white matter disease; space occupying lesions;

ApoE e4 homozygote

which is not controlled, or which requires treatment with biologic drugs

Untreated bleeding disorder, platelet count <50,000, or international normalized ratio (INR) >1.5

Thyroid stimulating hormone above normal range (TSH > 5 mU/L if < 65 years old; TSH > 7.5 mU/L if > 65 years old)

Low serum vitamin B12 level

Untreated human immunodeficiency virus (HIV)

Malignant neoplasm under active therapy

Answer "yes" to Columbia-Suicide Severity Rating Scale (C-SSRS) suicidal ideation Type 4 or 5, or any suicidal behavior assessment within the past 6 months

Hospitalized or treated for suicidal behavior in the past 5 years

Current substance use disorder or positive urine drug screen

Updated version may be found at [PBM INTERNET](#) or [PBM INTRANET](#)

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1.3K

Ash Paul @pash22 · Mar 16, 2023

@alzassociation lobbies @congressdotgov for @CMSGov & @MedicareGov coverage of Lecanemab and other drugs [reuters.com/business/health...](#) via @aabolenein Why the sudden hurry to circumvent forthcoming @US_FDA #ADCOM? Are they getting nervous?

reuters.com

Focus: Alzheimer's Association lobbies for Medic

The Alzheimer's Association has deployed 1,000 people diagnosed with, or caring for ...

2

4

883

Lon S. Schneider, MD @LonSchneiderMD · Mar 16, 2023

Who would rely on an Advisory Committee even if it's stacked and the questions are most likely

1

706

Lon S. Schneider, MD @LonSchneiderMD · Mar 16, 2023

Questions are most likely not going to about approval but rather about post marking or labeling or possibly a REMS.

1

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723

barttels @barttels2 · Mar 16, 2023

I'd watch the markets. Should tell you what people actually think.

1

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713

LogarithmicDis @LogarithmicDis · Mar 16, 2023

The markets indicate what investors think based on what it being promoted.

The markets do not reflect, at least initially, what real world experiences are until those are established in the media.

1

3

752

barttels @barttels2 · Mar 17, 2023

Yes.

But those people are putting actual money down, not just patter.

1

1

779

Ash Paul @pash22 · Mar 28, 2023

Scott @ayton_scott raises v imp issues in this meta-analysis which concludes brain volume loss in amyloid antibody trials is highly correlated with ARIA [twitter.com/ayton_scott/st...](#) HT @MadhavThambiset

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emergence of ARIA in some patients an early warning sign that they are at greater risk of worsening neurodegeneration & potentially worse long-term clinical outcomes?"
tinyurl.com/2uvx9akd @ProfRobHoward @pash22

3 2 6 1.8K

Chuck Gartland @ChuckGartland1 · Apr 3, 2023

If you are getting rid of amyloid does that not decrease volume? Less "stuff" = less volume?

2 1 820

Madhav Thambisetty @MadhavThambiset · Apr 3, 2023

This guy has way more expertise than me on this question @ayton_scott !

1 2 873

Ash Paul @pash22 · Apr 4, 2023

Blood biomarkers in Alz': ready for clinical practice? jnnp.bmj.com/content/early/... via @LizCoulthard et al

1 4 7 1.7K

LogarithmicDis @LogarithmicDis · Apr 4, 2023

I'm not sure of the utility of this very narrow review when we have mountains of biomarker studies out there - their utility also substantially varying. 🤔

1 1 973

Nicolas Villain @nvillain_alz · Apr 5, 2023

It's not a review but an Editorial Commentary, so it comments on the three studies published in the same JNNP issue; that's its goal. It's not intended to do more. 🧐

1 1 3 1.2K

Ash Paul @pash22 · Apr 5, 2023

Yup, the editorial also makes it crystal clear "In research cohorts, blood biomarkers offer high sensitivity and specificity for AD. However, we require real-world blood biomarker data before validating them for clinical use ..."

2 2 886


Jason Cohen @MemoryDoc · Apr 5, 2023

The blood based biomarker Q just got more concrete: NY State just authorized clinical use of a plasma AB42:40 test testdirectory.questdiagnostics.com/test/test-guid-... Getting PET or CSF around here is very, very hard. Maybe use this for select pts? What do you folks think?

6 2 995

Nicolas Villain @nvillain_alz · Apr 5, 2023

pTau is very much likely to be a better candidate for plasma biomarker in clinical practice: higher fold changes, higher robustness and so on



As a library, the National Library of Medicine (NLM) provides access to scientific literature.
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The accuracy and robustness of plasma biomarker models for amyloid P...

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2

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9

2K

Jason Cohen

@MemoryDoc · Apr 5, 2023

Right, but I can't choose which BBB are clinically available. I have only 1 option, so in very select pts w clinical uncertainty despite MRI, neuropsych, etc, where it may change mgmt, do I use the option? Or continue w standard of care, which is 🧐🧐🧐 & long explanations

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977

Nicolas Villain

@nvillain_alz · Apr 5, 2023

I am not sure, tbh... What you ask was well-documented with Amyloid PET (IDEAS+++ and other tertiary centers case series), with very good results (change in Dx and mgmt). Here, you have surrogate for amyloid PET with only Se and Sp~0.7-0.8. Not sure how helpful will that be 🧐

2

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982

Ash Paul

@pash22 · Apr 5, 2023

Hi Nicolas, I am slightly confused now, I was always taught as a Registrar that one needed to consider sensitivity, specificity, PPV and NPV in a biomarker/test gpsych.bmj.com/content/34/2/e... via @statsROC researchers

2

2

1.1K

David Rind

@dmrind · Apr 5, 2023

I would argue that diagnostic testing involves understanding at least test characteristics, target population, prevalence, disease spectrum, confirmatory testing, and effects on management, and so is among the most complex topics in clinical epidemiology and medicine.

2

11

1.9K

Ash Paul

@pash22 · Apr 17, 2023

US @icer_review Publishes Final Evidence Report on Lecanemab for Alzheimer's Disease [@myemail.constantcontact.com/ICER-Publishes...](https://myemail.constantcontact.com/ICER-Publishes...) @barttels2 @sadneurons

Lecanemab for Alzheimer's Disease

— Independent appraisal committee voted that currently available evidence is not adequate to demonstrate a net health benefit for lecanemab when compared to supportive care —

— Using best estimates from current data, ICER analyses suggest

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@Adrian_H

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lecanemab when compared to supportive care —

— Using best estimates from current data, ICER analyses suggest lecanemab would achieve common thresholds for cost-effectiveness if priced between \$8,900 – \$21,500 per year —

— Manufacturers should release all patient-level data to help patients, clinicians, researchers, and regulators understand more about

- 1

8

7

5.8K
- Lon S. Schneider, MD** @LonSchneiderMD · Apr 17, 2023

Let's see @icer_review says:
1. Lack of evidence showing benefits
2. But cost-effective at \$21.5K
3. Release individual patient data

No. 2 doesn't consider \$60K added charges for PET, MRI, infusion & medical visits.
No. 3 will never happen while drug is proprietary.

Solutions?

5

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1.6K
- David Rind** @dmrind · Apr 17, 2023

Not sure why people always point to the highest number when ICER gives a range. Could well argue for the low end of the range given uncertainties.
In any case, the analysis includes MRI and infusion costs, but not PET scans, since PET scans are part of diagnosis.

2

2

725
- Dave Weisman** @dcweisman · Apr 17, 2023

CSF does just as well.

1

663
- Jason Cohen** @MemoryDoc · Apr 18, 2023

True, but how often are you able to convince folks to get an LP, outside of rapidly progressive or suspected autoimmune?

2

724
- Nicolas Villain** @nvillain_alz · Apr 18, 2023

In France, where CSF (not PET) has been covered for more than 10 years, we do that every day, and it's pretty easy to convince people: will to know-increase the Dx certainty / will to anticipate the future-has a prognostic value / now Leqembi ;)

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769
- Ryan Townley** @DrTFromKC · Apr 18, 2023

Our current approach for cases that are not straightforward is FDG-PET ...

then CSF biomarkers if FDG is inconclusive.

Almost all are fine with getting LP. Ours are done by interventional radiology.

If it's the barrier to getting drug I don't see many turning that down.

3

2

745
- Dave Weisman** @dcweisman · Apr 18, 2023

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- Adrian H** @Adrian_H

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Dave Weisman @dcweisman · Apr 18, 2023
If it's the barrier to getting drug I don't see many turning that down.
3 2 745

Ryan Townley @DrTFromKC · Apr 18, 2023
Sounds like CSF with extra steps.
1 749

Ryan Townley @DrTFromKC · Apr 18, 2023
Absolutely disagree. You learn much more about differential diagnosis than you do with CSF.

Dave Weisman @dcweisman · Apr 18, 2023
3 2 7 972
OK, just trying to channel Rick Sanchez. My local read for 95-99% of above: indeterminate.

Trey Bateman @RenegadeSynapse · Apr 18, 2023
3 1 891
Can confirm. The FDG reads I've seen are terrible. Have seen bvFTD called because of hypomet that was, dear readers, the corpus callosum.
I got little experience with PET in training. Between a few exchanges with @DavidJonesBrain and @DrTFromKC I feel fairly confident.

Nicolas Villain @nvillain_alz · Apr 19, 2023
2 8 756
Can't agree more: I fell for FDG PET 15 years ago as a PhD student, and I still find it one of the most helpful tools in clinical practice. As you all underlined, it depends a lot on the expertise of the reader, but great tools can now help the Philistines!

Dave Weisman @dcweisman · Apr 19, 2023
3 2 759
Seen so many cases where it sowed more confusion, including yesterday: abnl PET (done for depression with MRI showing "atrophy") with currently normal cognition.

David Jones @DavidJonesBrain · Apr 19, 2023

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Adrian H @Adrian_H
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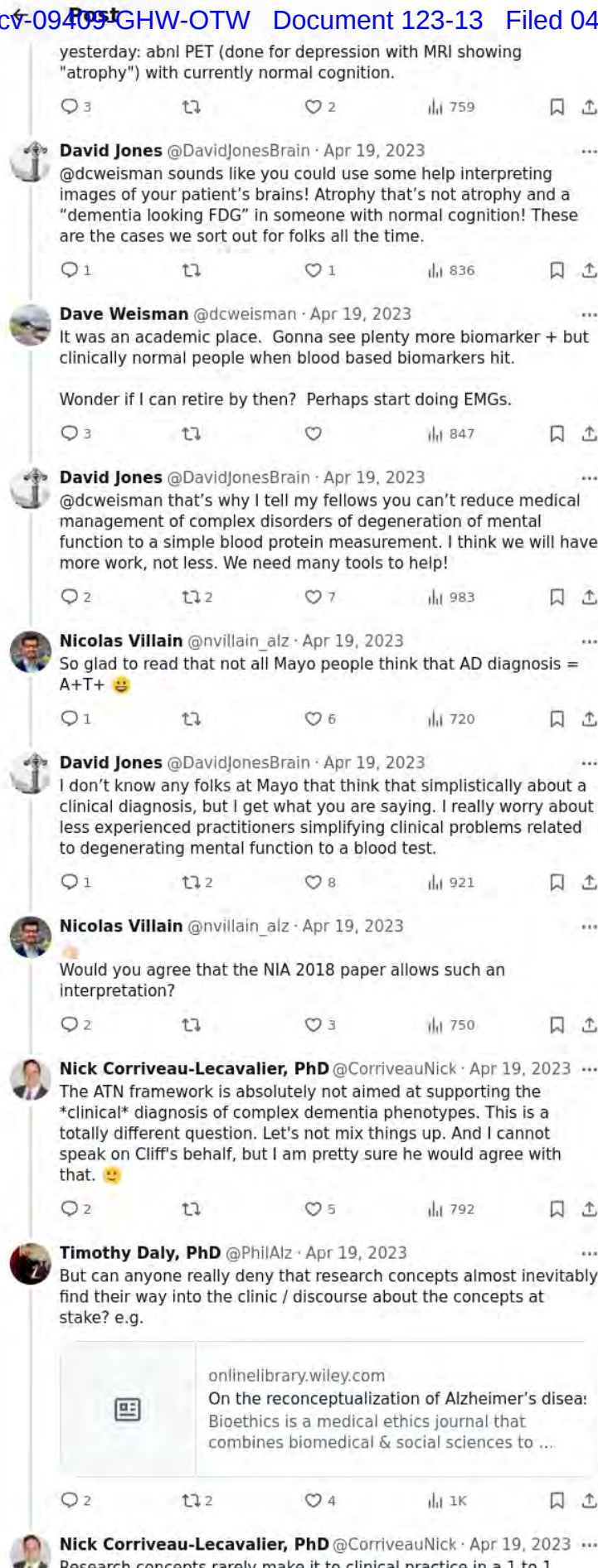
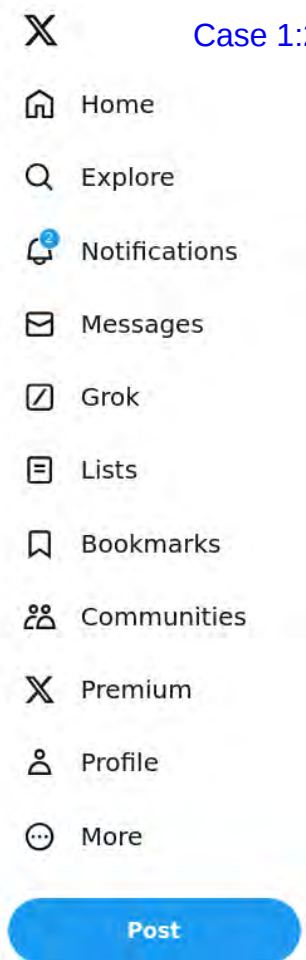
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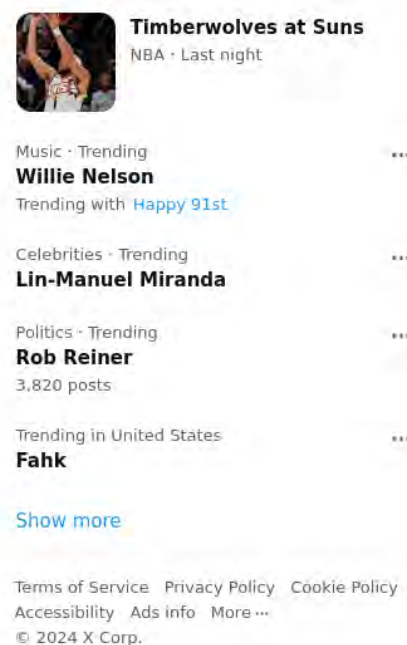
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Nick Corriveau-Lecavalier, PhD @CorriveauNick · Apr 19, 2023 ...
Research concepts rarely make it to clinical practice in a 1 to 1

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Nick Corriveau-Lecavalier, PhD @CorriveauNick · Apr 19, 2023 ...
Research concepts rarely make it to clinical practice in a 1 to 1 format. The ATN framework is aimed at a purely biological conceptualization of a disease. It influences clinical practice but a good clinician knows the clinico-pathological complexities of dementia syndromes.

3

5

753

Nicolas Villain @nvillain_alz · Apr 19, 2023 ...
Absolutely!
And there's a continuum to clinical practice: framework lead to new RCT designs, which, in case of approval, then directly translate into clinical practice

1

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692

Nick Corriveau-Lecavalier, PhD @CorriveauNick · Apr 19, 2023 ...
Yes I agree. But even if blood biomarkers successfully go through all of this, they would not answer all the necessary questions related to patient care, diagnosis, prognosis and counseling

2

723

Nicolas Villain @nvillain_alz · Apr 19, 2023 ...
Absolutely! It looks like we all deal with patients in a similar manner in this thread!
My tweet was provocative, not to make you uncomfortable and test your "corporateness", but to ask you, honestly, if this research framework might unvoluntarily lead to this undesired direction

2

4

725

Nick Corriveau-Lecavalier, PhD @CorriveauNick · Apr 19, 2023 ...
As David said the risk here is that unexperienced clinicians may think that ATN status is all you need to make a diagnosis. We are lucky to work in academic centers where people know that a progressive amnesic syndrome can be multifactorial and not always == AD path.

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6

732

Nicolas Villain @nvillain_alz · Apr 19, 2023 ...
Yes! In my opinion, the problem is more related to the opposite situation of your example: if we don't consider the phenotype anymore (which was the central message).Of course, A and T biology is central, but not the alpha and omega for all that. That's the risk of this framework

3

4

789

David Jones @DavidJonesBrain · Apr 19, 2023 ...
Yes! That's a poor implementation of a good framework. The framework is sound if used in proper clinical reasoning and serves research well as is.

1

5

722

Nicolas Villain @nvillain_alz · Apr 19, 2023 ...
Thanks to both of you for this constructive debate!
Last question, somehow in line with what we just debated: I would value your opinion on this large phase 3 RCT design?

clinicaltrials.gov/ct2/show/NCT05...

4

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766

Nicolas Villain @nvillain_alz · Apr 19, 2023 ...
(precisely the inclusion criteria)

1

722

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Nicolas Villain @nvillain_alz · Apr 19, 2023
(precisely the inclusion criteria)

Dave Weisman @dcweisman · Apr 19, 2023
They want to rapidly screen people with TICS, then do biomarker from blood. Implementation will be hard as these sites will have many screen fails.

Nicolas Villain @nvillain_alz · Apr 19, 2023
Thx David! My question was more about the definition and conception of AD, here: make a phone call and a blood test. Here you have your answer!

Dave Weisman @dcweisman · Apr 19, 2023
You must define AD based on amyloid for these prevention trials. And they are likely to live long enough to get it. It isn't like HTN as a rf for stroke.

Trey Bateman @RenegadeSynapse · Apr 19, 2023
It's a REALLY good risk factor, defined this way. Basically the debate about terminology between jack and Dubois at AAN last year

Nick Corriveau-Lecavalier, PhD @CorriveauNick · Apr 19, 2023
AD and AD dementia are not the same. You can have AD and be at risk for AD dementia simultaneously, according to these frameworks. I think we should ideally say "progressive amnestic syndrome" or something similar, but not AD dementia. This would save an ocean of ink.

Timothy Daly, PhD @PhilAlz · Apr 19, 2023
An undeniable tension between research concepts and clinical practice, no? Historically, AD = NeuroPathology+ and dementia. NIA says that NP+ people have symptomless disease. IWG 2021 says they're at risk of AD (understood clinically). IMO IWG is clearer + more grounded.

Joseph Therriault @JosephTherr · Apr 20, 2023
since 1997, neuropathological diagnosis of AD has not required symptoms, so this concept is not new

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Inclusion in an NLM database does not imply endorsement of, or agreement with, the contents by NLM or the National Institutes of Health.

A brief history of "Alzheimer disease": Multiple meanings separated by ...

From ncbi.nlm.nih.gov

Nicolas Villain @nvillain_alz · Apr 21, 2023

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A brief history of "Alzheimer disease": Multiple meanings separated by ...

From ncbi.nlm.nih.gov

5 1 3 803

Nicolas Villain @nvillain_alz · Apr 21, 2023

3/3

In 2012 the updated NIA guidelines stated that "There is consensus to disentangle the clinicopathologic term "Alzheimer's disease" from AD neuropathologic change" Neuropath were always very cautious in distinguishing the term disease from brain lesions

alz-journals.onlinelibrary.wiley.com

National Institute on Aging-Alzheimer's Associat

A consensus panel from the United States and Europe was convened recently to update and ...

1 1 2 698

Nicolas Villain @nvillain_alz · Apr 21, 2023

or, precisely in these 2012 guidelines, the term "Alzheimer's disease" from "Alzheimer's disease neuropathologic changes."

1 1 1 694

Ryan Townley @DrTFromKC · Apr 21, 2023

So if someone comes into the clinic with A+/T+/N+ with subjective cognitive impairment but they test cognitively normally on my test that day would you propose I tell them:

You have AD neuro pathologic change but good news is you don't have Alzheimer's disease!

2 1 724

Nicolas Villain @nvillain_alz · Apr 21, 2023

Absolutely, like someone who would come to your clinic with dyspnea, no acute vascular event detected, but significant atheroma and vascular risk factors. You're at high-risk, but you don't have any myocardial infarction. So let's start secondary prevention but no use of acute Rx

2 1 711

Ryan Townley @DrTFromKC · Apr 21, 2023

But we have counter examples in medicine with better success of curbing bad health outcomes.

If you have someone with HbA1c of 7.4 but normal creatinine and no neuropathy symptoms, we don't wait until they have those changes before we diagnose and treat their diabetes.

1 1 730

Nicolas Villain @nvillain_alz · Apr 21, 2023

Absolutely: some cancers as well. My point is the following: the only interest in clinical practice to do that is when you have Rx options. Here, unfortunately, not the case.

1 734

Ryan Townley @DrTFromKC · Apr 21, 2023

Correct. So the definition you are proposing suddenly changes once we have a treatment? Seems philosophically odd to me.

Like I get it, but I'm suggesting that I get both angles here and it's not so black and white to me.

1 1 745

Nicolas Villain @nvillain_alz · Apr 21, 2023

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Like I get it, but I'm suggesting that I get both angles here and it's not so black and white to me.

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745

Nicolas Villain @nvillain_alz · Apr 21, 2023

...

No, it's not, and in medicine, we use different philosophies to define diseases: look at the DSM! So, different situations, different options. Here, semantics hurt probably patients (you've AD!), so what we propose is to be careful!

1

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751

Ryan Townley @DrTFromKC · Apr 21, 2023

...

I think ignoring the pre-cognitive decline stages (lots of brain damage has now occurred) has done more harm to patients in finding proper treatments to curb actual dementia rates.

This will eventually change to look like my analogy below and I will eagerly await that day.

2

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806

Nicolas Villain @nvillain_alz · Apr 21, 2023

...

That's not what we say in IWG at all! Instead, to conduct research on these at-risk individuals. But, considering the debate regarding the deterministic vs probabilistic model of AD, the lack of Rx, it seems more reasonable to name them at-risk than having the disease in practice

2

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830

Ryan Townley @DrTFromKC · Apr 21, 2023

...

Yes - even on the research side when I do biomarker disclosure visits in our research participants I use "at risk" and discuss the reality that A+ changes occur over 10-20 years and many may never develop cognitive symptoms.

But I don't feel as honest saying that when A/T/N+

3

1

1.1K

LogarithmicDis @LogarithmicDis · Apr 22, 2023

...

For disclosing research results to patients, the CLIA certification process for labs and tests are here, according to law:

ecfr.gov/current/title-...

1

1

690

Ash Paul @pash22 · Apr 22, 2023

...

Here are the rules in England genomicsengland.co.uk/patients-parti... via @GenomicsEngland

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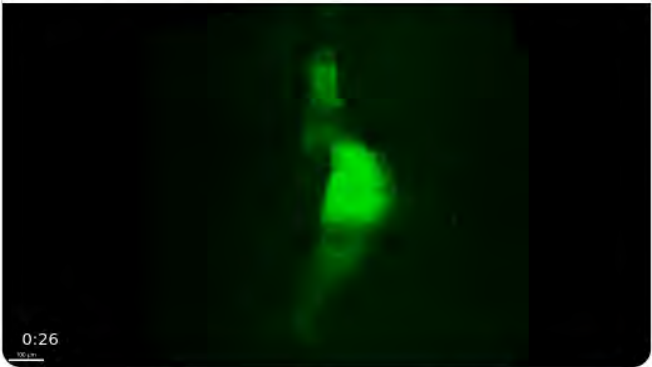
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1 1 760

Ash Paul @pash22 · Apr 22, 2023
Here's an interesting tweetorial from Matthew @schrag_matthew on the recent @cpiller story on Lecanemab

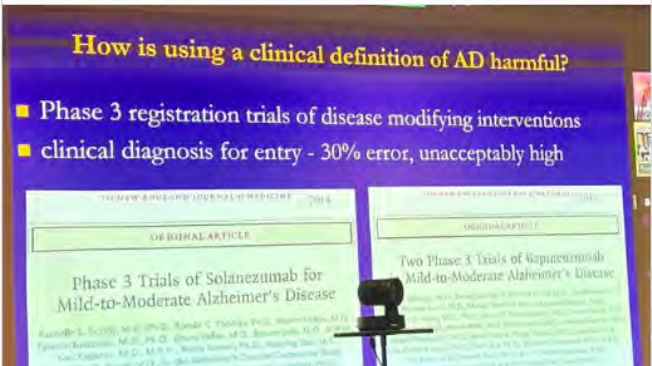
Matthew Schrag @schrag_matthew · Apr 13, 2023
We have had the incredible privilege of studying the brain of a patient who died after three doses of Lecanemab/Lequemi. This striking case has intense cerebrovascular inflammation/degeneration. We are so grateful to her family for sharing her story w the scientific community.



1 3 1.4K

LogarithmicDis @LogarithmicDis · Apr 22, 2023
Imagine the sponsor liability for a RCT patient having a brain bleed or death in a RCT who failed to adequately diagnose AD - or CAA.

Michael Okun @MichaelOkun · Apr 21, 2023
How can a lack of a biological definition of #alzheimers be harmful for clinical trials of disease modification. Cliff Jack at @MayoClinic nails it @movedisorder subtyping meeting.



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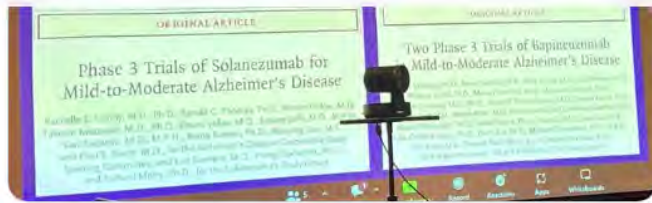
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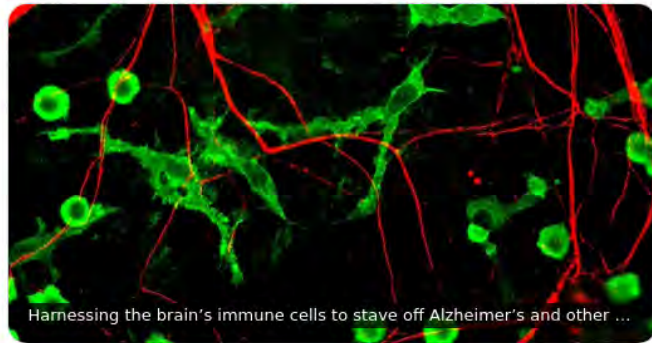
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1 1 1.2K



Ash Paul @pash22 · Apr 23, 2023
Harnessing the brain's immune cells to stave off Alzheimer's and other neurodegenerative diseases [theconversation.com/harnessing-the...](https://theconversation.com/harnessing-the-brains-immune-cells-to-stave-off-alzheimers-and-other-neurodegenerative-diseases) via @kzengeler



From theconversation.com
1 1 950



LogarithmicDis @LogarithmicDis · Apr 23, 2023
I'm firmly in the microglia camp.

1 1 952



Ash Paul @pash22 · Apr 24, 2023
The new face of Alzheimer's: Early stage patients who refuse to surrender [washingtonpost.com/health/2023/04/...](https://www.washingtonpost.com/health/2023/04/24/alzheimers-new-face-early-stage-patients-who-refuse-to-surrender/) via @LaurieMcGinley1



5 1K

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Robert Howard @ProfRobHoward · Apr 24, 2023
Also to exaggerate the benefits of lifestyle interventions in preventing decline in MCI. And these people who are writing books, 5 and 8 years post-diagnosis probably need to get their diagnosis re-evaluated.

4 2 4 1.7K



Ash Paul @pash22 · Apr 24, 2023



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preventing decline in MCI. And these people who are writing books, 5 and 8 years post-diagnosis probably need to get their diagnosis re-evaluated.

4 2 4 1.7K



Ash Paul @pash22 · Apr 24, 2023

"Lifestyle may affect your dementia risk but the extent is exaggerated: There are many things we can do to try to reduce our risk of dementia, but the condition is not usually preventable" archive.ph/NSTAN via @ClareWilsonMed



1 1 4 1.2K



Jamie Timmons @metapredict · Apr 24, 2023

What are those many things the individual can do to substantially reduce their risk? (blueberries, exercise, CBT, green-tea, yoga, omega-3 need not apply) - RCT data only please 🙏

1 1 874



Ash Paul @pash22 · Apr 24, 2023

Keep searching Jamie!
"Dementia risk reduction: why haven't the pharmacological risk reduction trials worked? An in-depth exploration of seven established risk factors" ncbi.nlm.nih.gov/pmc/articles/P... via @ruth_peters_ et al



From ncbi.nlm.nih.gov

1 1 2 971



Ash Paul @pash22 · Apr 24, 2023

Also chk out 'Evidence-based prevention of Alzheimer's disease: systematic review and meta-analysis of 243 observational prospective studies and 153 RCTs' jnnp.bmj.com/content/91/11/... via @brunovellas et al



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